

PjPμPSC€PsCñ PjC-CñPsCñ TyK2. Pk° PIC-PrPjC-PSCr PIC-Pr PSPëC..., C-PSC€C-
 PeC-PSP°P·Pë PI PiPμPSPsPjC- P»CñPrPëPSPë PSpμ P·P°P·PSP°CñC,CH PIPiP»PëPICr
 C,PsC,,P°C†PëC,PëPSC-P±C†. PJ PeP»C-C,PëPSP°C... P»CñPrPëPSPë C,PsC,,P°C†PëC,PëPSC-P±
 PiPμCñPμPIP°P¶PSPs PiCñPëPiPSC-C†C†C” PiPμCñPμPrP°C†C† C†PëPiPSP°P»C-PI
 PiPμC,PμCñPsPrPëPjPμCñPSPëPjPë CñPμC†PμPiC,PsCñP°PjPë C†PëC,PsPeC-PSC-PI, C¶PeC-
 P°C†PsC†C-CñCñC,CHC†C¶ P· JAK3 C,P°/P°P±Ps JAK1, C-P· C,,C†PSPeC†C-PsPSP°P»CHPSPsCñ
 C†PμP»PμPeC,PëPIPSC-C†C,Cñ C%PsPrPs CñPμC†PμPiC,PsCñC-PI C†PëC,PsPeC-PSC-PI,
 C¶PeC- PiPμCñPμPrP°CñC,CH C†PëPiPSP°P»Pë C†PμCñPμP· PiP°CñPë PeC-PSP°P· JAK2.
 P†PSPiC-P±C†PIP°PSPSC¶ JAK1 C- JAK3 C,PsC,,P°C†PëC,PëPSC-P±PsPj PiPsC†P»P°P±P»CñC”
 PiPμCñPμPrP°C†C† C†PëPiPSP°P»C-PI C-PSC,PμCñP»PμPñPeC-PSC-PI (IL-2, -4, -6, -7, -9, -15,
 -21) C,P° C-PSC,PμCñC,,PμCñPsPSC-PI C,PëPiC† I C- II, C%Ps PiCñPëP·PIPsPrPëC,CH PrPs
 PjPsPrC†P»C¶C†C-C— C-PjC†PSPSPsC— C,P° P·P°PiP°P»CHPSPsC— PIC-PrPiPsPIC-PrC-.

PαP°CñPjP°PePsPrPëPSP°PjC-C†PSP° PrC-C¶

PJ PiP°C†C-C”PSC,C-PI C-P· CñPμPIPjP°C,PsC—PrPSPëPj P°CñC,CñPëC,PsPj
 P»C-PeC†PIP°PSPSC¶ C,PsC,,P°C†PëC,PëPSC-P±PsPj PiCñPsC,C¶PiPsPj PiPμCñC-PsPrC† PrPs 6
 PjC-C†C¶C†C-PI P±C†P»Ps P°C†PsC†C-PñPsPIP°PSPμ P· PrPsP·PsP·P°P»PμP¶PSPëPj
 P·PSPëP¶PμPSPSC¶Pj PeC-P»CHPePsC†C,C- C†PëCñPeC†P»CñCñC†PëC... PeP»C-C,PëPS
 PiCñPëCñPsPrPSPëC... PeC-P»PμCñC-PI, PiPsP·PëC,PëPIPSPëC... P·P° CñPμC†PμPiC,PsCñP°PjPë
 CD16/56 , PiCñPëC†PsPjC†, P·P° PsC†C-PSPeP°PjPë, PjP°PeC†PëPjP°P»CHPSPμ
 P·PSPëP¶PμPSPSC¶ PeC-P»CHPePsC†C,C- C†PëC... PeP»C-C,PëPS PIC-PrP±C†PIP°P»PsC†C¶
 PiCñPëP±P»PëP·PSPs C†PμCñPμP· 8Bñ“10 C,PëP¶PSC-PI PiC-C†P»C¶ PiPsC†P°C,PeC†
 C,PμCñP°PiC-C—. PjC- P·PjC-PSPë P·P°P·PIPëC†P°Pñ P·PSPëPeP°P»Pë PiCñPsC,C¶PiPsPj
 2Bñ“6 C,PëP¶PSC-PI PiC-C†P»C¶ PiCñPëPiPëPSPμPSPSC¶ C,PμCñP°PiC-C—. PÿPμCñP°PiC-C¶
 C,PsC,,P°C†PëC,PëPSC-P±PsPj P±C†P»P° P°C†PsC†C-PñPsPIP°PSP° P· PrPsP·PsP·P°P»PμP¶PSPëPj
 P·P±C-P»CHC€PμPSPSC¶Pj PeC-P»CHPePsC†C,C- B-PeP»C-C,PëPS. P—PjC-PSPë PI
 PeC-P»CHPePsC†C,C- C†PëCñPeC†P»CñCñC†PëC... Pÿ-P»C-PjC,,PsC†PëC,C-PI C-
 PiC-PrPiCñC†Pi Pÿ-P»C-PjC,,PsC†PëC,C-PI (CD3 , CD4 C- CD8) P±C†P»Pë PSpμP·PSP°C†PSPëPjPë
 C,P° PSPμPiPsC†C,C-PñPSPëPjPë.

PμC-C†P»C¶ PrPsPIPiPsC†C,CñPsPePsPIPsC— C,PμCñP°PiC-C— (PjPμPrC-P°PSPSP°
 C,CñPëPIP°P»C-C†C,CH P»C-PeC†PIP°PSPSC¶ C,PsC,,P°C†PëC,PëPSC-P±PsPj
 C†C,P°PSPsPIPëC,CH PiCñPëP±P»PëP·PSPs 5 CñPsPeC-PI) PeC-P»CHPeC-C†C,CH CD4 C- CD8
 PeP»C-C,PëPS, C¶Pe P±C†P»Ps PiPsPeP°P·P°PSPs, P·PSPëP¶C†PIP°P»P°C†C¶ PI
 C†PμCñPμPrPSCñPsPjC† PSP° 28 C- 27 % PIC-PrPiPsPIC-PrPSPs, PIC-Pr PIPëC...C-PrPSPsPiPs
 CñC-PIPSC¶. Pk° PIC-PrPjC-PSCr PIC-Pr C†PiPsC†C,PμCñPμP¶C†PIP°PSPsPiPs
 P·PSPëP¶PμPSPSC¶ PiC-C†P»C¶ PePsCñPsC,PePsC†P°C†PSPsPiPs PrPsP·C†PIP°PSPSC¶,
 PeC-P»CHPeC-C†C,CH PiCñPëCñPsPrPSPëC... PeP»C-C,PëPS-PeC-P»PμCñC-PI CD16/56
 P·P±C-P»CHC€C†PIP°P»P°C†C¶ PSP° 73 % (PjPμPrC-P°PSPSPμ P·PSP°C†PμPSPSC¶) PIC-Pr
 PIPëC...C-PrPSPsPiPs CñC-PIPSC¶. PñC-P»CHPeC-C†C,CH CD19 P’-PeP»C-C,PëPS PSPμ
 PiCñPsPrPμPjPsPSC†C,CñC†PIP°P»P° PiPsPrP°P»CHC€PsPiPs P·P±C-P»CHC€PμPSPSC¶
 PiC-C†P»C¶ PrPsPIPiPsC†C,CñPsPePsPIPsPiPs P»C-PeC†PIP°PSPSC¶
 C,PsC,,P°C†PëC,PëPSC-P±PsPj. PJC†C- C†C- P·PjC-PSPμPSC- PiPsPeP°P·PSPëPePë PI
 PiC-PrPiCñC†PiP°C... P»C-PjC,,PsC†PëC,C-PI PiPsPIPμCñC,P°P»PëC†C¶ PrPs
 PIPëC...C-PrPSPsPiPs CñC-PIPSC¶ PiC-C†P»C¶ C,PëPjC†P°C†PsPIPsPiPs
 PiCñPëP·C†PiPëPSPμPSPSC¶ C,PμCñP°PiC-C—. PkPμPjP°C” P¶PiPsPrPSPëC... PrPsPeP°P·C-PI
 PiCñPëC†PëPSPSPs-PSP°C†P»C-PrPePsPIPsPiPs P·PiBñ™ C¶P·PeC† PjC-P¶ PeC-P»CHPeC-C†C,Cñ
 PiC-PrPiCñC†Pi P»C-PjC,,PsC†PëC,C-PI C- PIPëPSPëPePSPμPSPSC¶Pj C†PμCñPñPsP·PSPëC...
 P°P±Ps PsPiPsCñC,C†PSC-C†C,PëC†PSPëC... C-PSC,,PμPeC†C-Pñ C†Pë
 PsPiPμCñC-P·C†CñC†PsPiPs PiPμCñPiPμC†C† (C-PSC,,PsCñPjP°C†C-Cñ C%PsPrPs

PjPsPSC-C,PsC $\overline{H}$ P $\overline{P}$ SPiC $\acute{r}$ P°P±C $\acute{r}$ PsP»C $\overline{H}$ C,PSPsC— PeC-P»CHPePsC $\acute{r}$ C,C-
P»C-PjC,,PsC $\dagger$ P $\overline{P}$ C,C-PI PrP $\overline{P}$ PI. C $\acute{r}$ C $\overline{H}$ PsP·PrC-P»C- B«P $\overline{Y}$ PiPsC $\acute{r}$ C-P±
P·P°C $\acute{r}$ C,PsC $\acute{r}$ C $\acute{r}$ PIP°PSPSC $\downarrow$ C,P° PrPsP·P $\overline{B}$ »).

P—PjC-PSP $\overline{P}$ P·P°PiP°P»CH $\overline{P}$ SP $\overline{P}$ C... C $\overline{H}$ C-PIPSC-PI C-PjC $\acute{r}$ PSPsPiP»PsP±C $\acute{r}$ P»C-PSC-PI IgG, IgM
C,P° IgA PI C $\acute{r}$ P $\overline{P}$ C $\overline{H}$ PsPIP°C,C $\dagger$ C- PeC $\overline{H}$ PsPIC- PiC $\overline{H}$ PsC,C $\downarrow$ PIPsPj 6-PjC-C $\acute{r}$ C $\downarrow$ C $\dagger$ PSPsPiPs
PrPsP·C $\acute{r}$ PIP°PSPSC $\downarrow$ C,PsC,,P°C $\dagger$ P $\overline{P}$ C,P $\overline{P}$ SC-P±C $\acute{r}$ PI PiP°C $\dagger$ C-C''PSC,C-PI C-P·
C $\overline{H}$ PuPIPIjP°C,PsC—PrPSP $\overline{P}$ Pj P°C $\overline{H}$ C,C $\overline{H}$ P $\overline{P}$ C,PsPj (P Ph) P±C $\acute{r}$ P»P $\overline{P}$ PSPuPIPIuP»P $\overline{P}$ PeP $\overline{P}$ PjP $\overline{P}$, PSPu
P·P°P»PuP $\overline{P}$ °P»P $\overline{P}$ PIC-Pr PrPsP·P $\overline{P}$ C,P° P±C $\acute{r}$ P»P $\overline{P}$ PiPsPrC-P±PSP $\overline{P}$ PjP $\overline{P}$ PrPs C,P $\overline{P}$ C..., C $\downarrow$ PeC-
C $\acute{r}$ PiPsC $\acute{r}$ C,PuC $\overline{H}$ C-PiP°P»P $\overline{P}$ C $\acute{r}$ C $\downarrow$ PiC-Pr C $\dagger$ P°C $\acute{r}$ P·P°C $\acute{r}$ C,PsC $\acute{r}$ C $\acute{r}$ PIP°PSPSC $\downarrow$ PiP»P°C $\dagger$ PuP±Ps,
C%Ps PIPeP°P·C $\acute{r}$ C'' PSP° PIC-PrC $\acute{r}$ C $\acute{r}$ C,PSC-C $\acute{r}$ C,CH C $\acute{r}$ P $\overline{P}$ C $\acute{r}$ C,PuPjPSPsC—
C $\acute{r}$ C $\acute{r}$ PiC $\overline{H}$ PuC $\acute{r}$ C-C— PiC $\acute{r}$ PjPsC $\overline{H}$ P°P»CH $\overline{P}$ SPsPiPs C-PjC $\acute{r}$ PSC-C,PuC,C $\acute{r}$.

PuC-C $\acute{r}$ P»C $\downarrow$ P»C-PeC $\acute{r}$ PIP°PSPSC $\downarrow$ C,PsC,,P°C $\dagger$ P $\overline{P}$ C,P $\overline{P}$ SC-P±PsPj C $\acute{r}$ PiP°C $\dagger$ C-C''PSC,C-PI C-P·
P Ph C $\acute{r}$ PiPsC $\acute{r}$ C,PuC $\overline{H}$ C-PiP°P»PsC $\acute{r}$ C $\downarrow$ C $\overline{P}$ IP $\overline{P}$ PrPePu P·PSP $\overline{P}$ P $\overline{P}$ PIPSPSC $\downarrow$ C $\overline{H}$ C-PIPSC $\downarrow$
P $\overline{Y}$ -C $\overline{H}$ PuP°PeC,P $\overline{P}$ IPSPsPiPs P±C-P»PeP° (P $\overline{Y}$ P P') C $\acute{r}$ C $\acute{r}$ P $\overline{P}$ C $\overline{H}$ PsPIP°C,C $\dagger$ C- PeC $\overline{H}$ PsPIC-, C $\downarrow$ PePu
P·P±PuC $\overline{H}$ C-PiP°P»PsC $\acute{r}$ C $\downarrow$ PiC $\overline{H}$ PsC,C $\downarrow$ PIPsPj C $\acute{r}$ C $\acute{r}$ CH $\overline{P}$ sPiPs PiPuC $\overline{H}$ C-PsPrC $\acute{r}$
P»C-PeC $\acute{r}$ PIP°PSPSC $\downarrow$. PuPsPeP°P·PSP $\overline{P}$ PeP $\overline{P}$ C $\overline{H}$ C-PIPSC $\downarrow$ P $\overline{Y}$ P P', P·PjC-PSP $\overline{P}$ C $\acute{r}$ C $\downarrow$ PeP $\overline{P}$ C...
PIC-PrPjC-C $\dagger$ P°P»P $\overline{P}$ C $\acute{r}$ C $\downarrow$ PiC $\overline{H}$ PsC,C $\downarrow$ PIPsPj P»C-PeC $\acute{r}$ PIP°PSPSC $\downarrow$ PiC $\overline{H}$ PuPiP°C $\overline{H}$ P°C,PsPj
P $\overline{H}$ C $\acute{r}$ PuP»CHC $\downarrow$ IPSP·, PSPu PiPsPIPuC $\overline{H}$ C,P°P»P $\overline{P}$ C $\acute{r}$ C $\downarrow$ PiPsPIPSC-C $\acute{r}$ C,CH PrPs
PIP $\overline{P}$ C...C-PrPSPsPiPs C $\overline{H}$ C-PIPSC $\downarrow$ PiC $\overline{H}$ PsC,C $\downarrow$ PIPsPj 2 C,P $\overline{P}$ P $\overline{P}$ SC-PI PiC-C $\acute{r}$ P»C $\downarrow$
PiC $\overline{H}$ P $\overline{P}$ IP $\overline{P}$ SPuPSPSC $\downarrow$ C,PuC $\overline{H}$ P°PiC-C—, C%Ps PIPeP°P·C $\acute{r}$ C'' PSP° P±C-P»CHC $\overline{P}$ C $\acute{r}$
C,C $\overline{H}$ P $\overline{P}$ IP°P»C-C $\acute{r}$ C,CH C,,P°C $\overline{H}$ PjP°PePsPrP $\overline{P}$ SP°PjC-C $\dagger$ PSPsC— P°PeC,P $\overline{P}$ IPSPsC $\acute{r}$ C,C-
PiPsC $\overline{H}$ C-PIPSC $\downarrow$ IPSPs P· PiPuC $\overline{H}$ C-PsPrPsPj PSP°PiC-PIPIP $\overline{P}$ IPuPrPuPSPSC $\downarrow$.

P $\overline{H}$ P°C $\overline{H}$ PjP°PePsPeC-PSPuC,P $\overline{P}$ PeP°.

P $\overline{H}$ P°C $\overline{H}$ PjP°PePsPeC-PSPuC,P $\overline{P}$ C $\dagger$ PSP $\overline{P}$ PN $\overline{P}$ PiC $\overline{H}$ PsC,,C-P»CH C,PsC,,P°C $\dagger$ P $\overline{P}$ C,P $\overline{P}$ SC-P±C $\acute{r}$
C...P°C $\overline{H}$ P°PeC,PuC $\overline{H}$ P $\overline{P}$ ·C $\acute{r}$ C''C,CHC $\acute{r}$ C $\downarrow$ C $\overline{P}$ IP $\overline{P}$ PrPeP $\overline{P}$ j PIC $\acute{r}$ PjPsPeC,C $\acute{r}$ PIP°PSPSC $\downarrow$ Pj
(PjP°PeC $\acute{r}$ P $\overline{P}$ jP°P»CH $\overline{P}$ SP° PePsPSC $\dagger$ PuPSC,C $\overline{H}$ P°C $\dagger$ C-C $\downarrow$ PI PiP»P°P·PjC-
PrPsC $\acute{r}$ C $\downarrow$ PIP°C''C,CHC $\acute{r}$ C $\downarrow$ PiC $\overline{H}$ PsC,C $\downarrow$ PIPsPj 0,5b $\overline{H}$ "1 PiPsPrP $\overline{P}$ SP $\overline{P}$), C $\overline{P}$ IP $\overline{P}$ PrPeP $\overline{P}$ j
PIP $\overline{P}$ IPuPrPuPSPSC $\downarrow$ Pj (PiPuC $\overline{H}$ C-PsPr PSP°PiC-PIPIP $\overline{P}$ IPuPrPuPSPSC $\downarrow$ C $\acute{r}$ C,P°PSPsPIP $\overline{P}$ C,CH
~ 3 PiPsPrP $\overline{P}$ SP $\overline{P}$) C- PrPsP·PsPiC $\overline{H}$ PsPiPsC $\overline{H}$ C $\dagger$ C-PN $\overline{P}$ SP $\overline{P}$ j P·P±C-P»CHC $\overline{P}$ IPuPSPSC $\downarrow$ Pj
C $\acute{r}$ P $\overline{P}$ C $\acute{r}$ C,PuPjPSPsC— PuPeC $\acute{r}$ PiPsP·P $\overline{P}$ C $\dagger$ C-C—. P C-PIPSPsPIP°P $\overline{P}$ SC-
PePsPSC $\dagger$ PuPSC,C $\overline{H}$ P°C $\dagger$ C-C— PrPsC $\acute{r}$ C $\downarrow$ PIP°C $\overline{H}$ C,CHC $\acute{r}$ C $\downarrow$ PiC $\overline{H}$ PsC,C $\downarrow$ PIPsPj
24b $\overline{H}$ "48 PiPsPrP $\overline{P}$ SP C-P· PSPuP·PSP°C $\dagger$ PSPsC $\overline{H}$ PeC $\acute{r}$ PjC $\acute{r}$ P»C $\downarrow$ C $\dagger$ C-C''C $\overline{H}$ PiC $\overline{H}$ PuPiP°C $\overline{H}$ P°C,C $\acute{r}$
PiC-C $\acute{r}$ P»C $\downarrow$ P·P°C $\acute{r}$ C,PsC $\acute{r}$ C $\acute{r}$ PIP°PSPSC $\downarrow$ PrPIP° C $\overline{H}$ P°P·P $\overline{P}$ PSP° PrPsP±C $\acute{r}$.

B PhP±C $\acute{r}$ PsC $\overline{H}$ P±C $\dagger$ C-C $\downarrow$ C- C $\overline{H}$ PsP·PiPsPrC-P»

P $\overline{Y}$ PsC,,P°C $\dagger$ P $\overline{P}$ C,P $\overline{P}$ SC-P± PrPsP±C $\overline{H}$ Pu PIC $\acute{r}$ PjPsPeC,C $\acute{r}$ C''C,CHC $\acute{r}$ C $\downarrow$, PN $\overline{P}$ PsPiPs
P±C-PsPrPsC $\acute{r}$ C,C $\acute{r}$ PiPSC-C $\acute{r}$ C,CH PiC $\overline{H}$ P $\overline{P}$ PiPuC $\overline{H}$ PsC $\overline{H}$ P°P»CH $\overline{P}$ SPsPjC $\acute{r}$
B P·P°C $\acute{r}$ C,PsC $\acute{r}$ C $\acute{r}$ PIP°PSPSC- C $\acute{r}$ C,P°PSPsPIP $\overline{P}$ C,CH 74 %. P—P°C $\acute{r}$ C,PsC $\acute{r}$ C $\acute{r}$ PIP°PSPSC $\downarrow$
C,PsC,,P°C $\dagger$ P $\overline{P}$ C,P $\overline{P}$ SC-P±C $\acute{r}$ C $\overline{H}$ P°P·PsPj C-P· C—P $\overline{P}$ IPuCH P· PIP $\overline{P}$ C $\acute{r}$ PsPeP $\overline{P}$ j PIPjC-C $\acute{r}$ C,PsPj
P $\overline{P}$ P $\overline{P}$ C $\overline{H}$ C $\acute{r}$ PSPu PiC $\overline{H}$ P $\overline{P}$ ·PIPsPrP $\overline{P}$ »Ps PrPs P·PjC-PS P·PSP°C $\dagger$ PuPSC $\overline{H}$ AUC, C,PsPrC- C $\downarrow$ Pe
P·PSP°C $\dagger$ PuPSPSC $\downarrow$ C $\max$ P·PSP $\overline{P}$ P $\overline{P}$ C $\acute{r}$ PIP°P»P $\overline{P}$ C $\acute{r}$ C $\downarrow$ PSP° 32 %. Pj PeP»C-PSC-C $\dagger$ PSP $\overline{P}$ C...
PrPsC $\acute{r}$ P»C-PrP $\overline{P}$ IPuPSPSC $\downarrow$ C... C,PsC,,P°C $\dagger$ P $\overline{P}$ C,P $\overline{P}$ SC-P± P·P°C $\acute{r}$ C,PsC $\acute{r}$ PsPIC $\acute{r}$ PIP°P»P $\overline{P}$
PSPuP·P°P»PuP $\overline{P}$ IPSPs PIC-Pr PiC $\overline{H}$ P $\overline{P}$ PN $\overline{P}$ PsPjC $\acute{r}$ C—P $\overline{P}$ C-.

PuC-C $\acute{r}$ P»C $\downarrow$ PIPSC $\acute{r}$ C,C $\overline{H}$ C-C $\overline{P}$ SPCH $\overline{P}$ sPIPIuPSPSPsPiPs PIPIuPrPuPSPSC $\downarrow$ PiC $\overline{H}$ PuPiP°C $\overline{H}$ P°C,C $\acute{r}$
PsP±b $\overline{H}$ "C''Pj C $\overline{H}$ PsP·PiPsPrC-P»C $\acute{r}$ C $\acute{r}$ C,P°PSPsPIP $\overline{P}$ C,CH 87 P». PuC $\overline{H}$ P $\overline{P}$ ±P»P $\overline{P}$ ·PSPs 40 %
C $\dagger$ P $\overline{P}$ C $\overline{H}$ PeC $\acute{r}$ P»C $\overline{H}$ C $\dagger$ PsPiPs C,PsC,,P°C $\dagger$ P $\overline{P}$ C,P $\overline{P}$ SC-P±C $\acute{r}$ P·Pi $\overline{H}$ " C $\downarrow$ P·C $\acute{r}$ C''C,CHC $\acute{r}$ C $\downarrow$ P·

P±C-P»PeP°PjPë PīP»P°P·PjPë PeCḡPsPIC-. PŷPsC,,P°C†PëC,PëPSC-P±
P·PIBḡ™ CḡP·CrC"C,CHCḡCḡ PīPμCḡPμPIP°PḡPSPs P· P°P»CHP±CrPjC-PSPsPj C-,
PNḡPjPsPIC-CḡPSPs, PSPμ P·PIBḡ™ CḡP·CrC"C,CHCḡCḡ P· a1-PePëCḡP»PëPj
PiP»C-PePsPīCḡPsC,PμC—PSPsPj. PŷPsC,,P°C†PëC,PëPSC-P± CḡC-PIPSPsPjC-CḡPSPs
CḡPsP·PiPsPrC-P»CḡC"C,CHCḡCḡ PjC-Pḡ PμCḡPëC,CḡPsC†PëC,P°PjPë PNḡ PīP»P°P·PjPsCḡ.

P'C-PsC,CḡP°PSCḡC,,PsCḡPjP°C†C-Cḡ C,P° PIPëPIPμPrPμPSPSCḡ

PḡPμC...P°PSC-P·PjPë PeP»C-CḡPμPSCḡCḡ C,PsC,,P°C†PëC,PëPSC-P±Cr C" C,P°PePëPjPë:
PīCḡPëP±P»PëP·PSPs 70 % PīCḡPëPNḡPSCḡC,PSC— PrPsP·Pë PīCḡPμPīP°CḡP°C,Cḡ
PjPμC,P°P±PsP»C-P·CrC"C,CHCḡCḡ PI PīPμC†C-PSC†C- C,P° 30 % PIPëPIPsPrPëC,CHCḡCḡ
PSPëCḡPeP°PjPë PI PSPμP·PjC-PSPμPSPsPjCḡ PIPëPiP»CḡPrC-. PḡPμC,P°P±PsP»C-P·Pj
C,PsC,,P°C†PëC,PëPSC-P±Cr PsPīPsCḡPμCḡPμPrPePsPICḡC"C,CHCḡCḡ PīPμCḡPμPIP°PḡPSPs
C-P·PsC,,PμCḡPjPμPSC,PSPj CYP3A4 P· PSPμP·PSP°C†PSPsCḡ CrC†P°CḡC,Cḡ
C-P·PsC,,PμCḡPjPμPSC,Cḡ CYP2C19. Pj PrPsCḡP»C-PrPḡPμPSPSC- C,PsC,,P°C†PëC,PëPSC-P±Cr,
PjC-C†PμPSPsPiPs CḡP°PrC-PsP°PeC,PëPIPSPsCḡ PjC-C,PePsCḡ, Cr P»CḡPrPëPSPë
P±C-P»CHCḡPμ 65 % P·P°PiP°P»CHPSPsC— C†PëCḡPeCḡP»CḡCḡC†PsC—
CḡP°PrC-PsP°PeC,PëPIPSPsCḡC,C- PīCḡPëPīP°PrP°P»Ps PSP° PSPμP·PjC-PSPμPSPëPNḡ
C,PsC,,P°C†PëC,PëPSC-P±, P° CḡPμCḡC,Cḡ 35 % P±CrP»Ps PIC-PrPSPμCḡPμPSPs PSP°
CḡP°C...CḡPSPsPe 8 PjPμC,P°P±PsP»C-C,C-PI, PSP° PePsPḡPμPS P· CḡPePëC... PīCḡPëPīP°PrP°C"
PjPμPSCḡPμ 8 % P·P°PiP°P»CHPSPsC— CḡP°PrC-PsP°PeC,PëPIPSPsCḡC,C-. PjCḡC-
PjPμC,P°P±PsP»C-C,Pë CḡPīPsCḡC,PμCḡC-PiP°P»PëCḡCḡ Cr C,PIP°CḡPëPS C-, P·P°
PīCḡPsPiPSPsP·P°PjPë, PIPsPSPë PjP°C,PëPjCḡC,CH PjPμPSCḡ PSC-Pḡ 10-PeCḡP°C,PSCḡ
PμC,,PμPeC,PëPIPSC-CḡC,CH PīPsCḡC-PIPSCḡPSPs P· PSPμP·PjC-PSPμPSPëPj
C,PsC,,P°C†PëC,PëPSC-P±PsPj CḡC,PSCḡPsPIPSPs C-PSPiC-P±CrPIP°PSPSCḡ JAK1/3.
P-PsPrPSPëC... PrPsPeP°P·C-PI CḡC,PμCḡPμPsPePsPSPiPμCḡCḡC— PI P·CḡP°P·PeP°C... Cr
P»CḡPrPëPSPë PIPëCḡPIP»PμPSPs PSPμ P±CrP»Ps. PḡP°CḡPjP°PePsP»PsPiC-C†PSP°
P°PeC,PëPIPSC-CḡC,CH C,PsC,,P°C†PëC,PëPSC-P±Cr PīPsPIBḡ™ CḡP·P°PSP° P·
PIPëC...C-PrPSPsCḡ PjPsP»PμPeCḡP»PsCḡ. *In vitro* C,PsC,,P°C†PëC,PëPSC-P± C"
CḡCḡP±CḡC,CḡP°C,PSPj PrP»Cḡ PīPμPSP° PjPSPsPḡPëPSPSPsC— P»C-PeP°CḡCḡCHPePsC—
CḡPμP·PëCḡC,PμPSC,PSPsCḡC,C--1 (MDR1), P°P»Pμ PSPμ PrP»Cḡ P±C-P»PeP°
CḡPμP·PëCḡC,PμPSC,PSPsCḡC,C- CḡP°PeCḡ PjPsP»PsC†PSPsC— P·P°P»PsP·Pë (BCRP),
C,CḡP°PSCḡPīPsCḡC,PSPëC... PīPsP»C-PīPμPīC,PëPrC-PI PsCḡPiP°PSC-C†PSPëC...
P°PSC-PsPSC-PI (OATP1B1/1B3) P°P±Ps C,CḡP°PSCḡPīPsCḡC,PμCḡC-PI
PsCḡPiP°PSC-C†PSPëC... PeP°C,C-PsPSC-PI (OCT1/2).

PḡP°CḡPjP°PePsPeC-PSPμC,PëPeP° PI PīP°C†C-C"PSC,C-PI

PḡPμCḡPjPμPSC,P°C,PëPIPSP° P°PeC,PëPIPSC-CḡC,CH C-P·PsC,,PμCḡPjPμPSC,C-PI
CḡPëCḡC,PμPjPë CYP Cr PīP°C†C-C"PSC,C-PI C-P· P Pḡ P·PSPëPḡCḡC"C,CHCḡCḡ C†PμCḡPμP·
C...CḡPsPSC-C†PSPμ P·P°PīP°P»PμPSPSCḡ. Pj PīP°C†C-C"PSC,C-PI C-P· P Pḡ PeP»C-CḡPμPSCḡ
C,PsC,,P°C†PëC,PëPSC-P±Cr PīCḡPë PīPμCḡPsCḡP°P»CHPSPsPjCḡ P·P°CḡC,PSCḡCḡPIP°PSPSC-
PSPμ P·PjC-PSCḡC"C,CHCḡCḡ C-P· C†P°CḡPsPj, C%Ps PIPeP°P·CrC" PSP° C,Pμ, C%Ps
C,PμCḡP°PīC-Cḡ C,PsC,,P°C†PëC,PëPSC-P±PsPj PSPμ PSPsCḡPjP°P»C-P·CrC"
P°PeC,PëPIPSC-CḡC,CH C-P·PsC,,PμCḡPjPμPSC,C-PI CḡPëCḡC,PμPjPë CYP.

PμPsPīCḡP»CḡC†C-PNḡPSPëPNḡ C,,P°CḡPjP°PePsPeC-PSPμC,PëC†PSPëPNḡ (PḡPḡ) P°PSP°P»C-P· Cr
PīP°C†C-C"PSC,C-PI C-P· P Pḡ PīCḡPsPrPμPjPsPSC,CḡCḡPIP°PI, C%Ps CḡPëCḡC,PμPjPSP°
PμPeCḡPīPsP·PëC†C-Cḡ (AUC) C,PsC,,P°C†PëC,PëPSC-P±Cr PīCḡPë PjPμPḡPsPIPëC...
P·PSP°C†PμPSPSCḡC... PrC-P°PīP°P·PsPSCḡ PjP°CḡPë C,C-P»P° (40 PePi; 140 PePi) P±CrP»P°
P°PSP°P»PsPiC-C†PSPsCḡ (C-P· PIC-PrC...PëP»PμPSPSCḡPjPë PI PjPμPḡP°C... 5 %) PrPs
C,P°PePsC— PI PīP°C†C-C"PSC,P° P· PjP°CḡPsCḡ C,C-P»P° 70 PePi. P—P° PsC†C-PSPeP°PjPë, Cr

P»C-C,PSC-C... PĪP°C†C-C" PSC,C-PI PIC-PePsPj 80 CĤPsPeC-PI P·PSP°C†PμPSPSCĬ AUC P±C†P»Pē PjPμPSC€ PSC-P¶ PSP° 5 % PIPëC‰PēPjPē PĪPsCĤC-PI PSCĬPSPs P· C,P°PePēPjPē P·PSP°C†PμPSPSCĬPjPē PI PĪP°C†C-C" PSC,C-PI PIC-PePsPj C† C†PμCĤPμPrPSCĤPsPjC† 55 CĤPsPeC-PI. Pj P¶C-PSPsPe PsC†C-PSPsC†PSC- P·PSP°C†PμPSPSCĬ AUC P±C†P»Pē PSP° 7 % PSPēP¶C†PēPjPē PĪPsCĤC-PI PSCĬPSPs C-P· PIC-PrPĪPsPIC-PrPSPēPjPē PĪPsPeP°P·PSPēPeP°PjPē C† C†PsP»PsPIC-PeC-PI. PĶP°CĬPI PSC- PrP°PSC- C,P°PePsP¶ C†PeP°P·C†CĤC,CH, C‰Ps PSPμPjP°C" C-C†C,PsC,PSPēC... PIC-PrPjC-PSPSPsC†C,PμPNē C† P·PSP°C†PμPSPSCĬC... AUC C,PsC,,P°C†PēC,PēPSC-P±C† PI PĪP°C†C-C" PSC,C-PI C"PICĤPsPĪPμPsC—PrPSPsC—, PSPμPiCĤPsC—PrPSPsC— C,P° PjPsPSPiPsP»PsC—PrPSPsC— CĤP°C†.

PŸPĪPsC†C,PμCĤC-PiP°PIC†CĬ PĪCĤPēP±P»PēP·PSPs P»C-PSC-PNēPSPēPNē P·PiBĤ™ CĬP·PsPe PjC-P¶ PjP°C†PsCĤ C,C-P»P° C,P° PsP±BĤ™ C" PjPsPj CĤPsP·PĪPsPrC-P»C†, C‰Ps PĪCĤPēP·PIPsPrPēP»Ps PrPs PIPëC‰PēC... P·PSP°C†PμPSCĤ PjP°PeC†PēPjP°P»CHPSPsC— PePsPSC†PμPSC,CĤP°C†C-C— (C_{max}) C- PSPēP¶C†PēC... P·PSP°C†PμPSCĤ P·P°P»PēC€PePsPIPsC— PePsPSC†PμPSC,CĤP°C†C-C— (C_{min}) C† PĪP°C†C-C" PSC,C-PI C-P· PSPμPIPμP»PēPePsCĤ PjP°C†PsCĤ C,C-P»P°. PhPrPSP°Pe C,P°PeP° PIC-PrPjC-PSPSC-C†C,CH PSPμ PIPiP°P¶P°C"C,CHC†CĬ PeP»C-PSC-C†PSPs P·PSP°C†C†C‰PsCĤ.

PĤC-P¶C-PSPrPēPIC-PrC†P°P»CHPSP° PIP°CĤC-P°P±PμP»CHPSC-C†C,CH (PePsPμC,,C-C†C-C" PSC, PIP°CĤC-P°C†C-C— C† PIC-PrC†PsC,PeP°C...) PrP»CĬ P·PSP°C†PμPSCĤ AUC C,PsC,,P°C†PēC,PēPSC-P±C† PsC†C-PSCĤPIP°P»P°C†CĬ PĪCĤPēP±P»PēP·PSPs C† 27 %.

P PμP·C†P»CHC,P°C,Pē PĪPsPiC†P»CĬC†C-PNēPSPsPiPs PαPĤ P°PSP°P»C-P·C† C† PĪP°C†C-C" PSC,C-PI C-P· P°PeC,PēPI PSPēPj PĪC†PsCĤC-P°C,PēC†PSPēPj P°CĤC,CĤPēC,PsPj, P° C,P°PePsP¶ C-P· PIPëCĤP°P·PePsPIPēPj PePsP»C-C,PsPj C†Pē P°PSPeC-P»Ps·C†CĤC†PēPj C†PĪPsPSPrC-P»C-C,PsPj PĪPsPjC-CĤPSPsPiPs P°P±Ps C,CĬP¶PePsPiPs C†C,C†PĪPμPSCĤ C†P·PiPsPrP¶C†PIP°P»PēC†CĬ P· C,P°PePēPjPē C† PĪP°C†C-C" PSC,C-PI C-P· P Ph.

PĶPēCĤPePsPIP° PSPμPrPsC†C,P°C,PSC-C†C,CH

Pj PĪP°C†C-C" PSC,C-PI C-P· P»PμPiPePsCĤ (PeP»C-CĤPμPSC† PeCĤPμP°C,PēPSC-PSC† 50BĤ"80 PjP»/C...PI), PĪPsPjC-CĤPSPsCĤ (PeP»C-CĤPμPSC† PeCĤPμP°C,PēPSC-PSC† 30BĤ"49 PjP»/C...PI) C- C,CĬP¶PePsCĤ (PeP»C-CĤPμPSC† PeCĤPμP°C,PēPSC-PSC† < 30 PjP»/C...PI) PSPēCĤPePsPIPsCĤ PSPμPrPsC†C,P°C,PSC-C†C,CH P·PSP°C†PμPSPSCĬ AUC P±C†P»Pē PIC-PrPĪPsPIC-PrPSPs PSP° 37 %, 43 % C- 123 % PIPëC‰PēPjPē, PSC-P¶ C† PĪP°C†C-C" PSC,C-PI P· PSPsCĤPjP°P»CHPSPsCĤ C,,C†PSPeC†C-C" CĤ PSPēCĤPsPe (PrPēPI. CĤPsP·PrC-P» B«PŸPĪPsC†C-P± P·P°C†C,PsC†C†PIP°PSPSCĬ C,P° PrPsP·PēB»).

Pj PĪP°C†C-C" PSC,C-PI C-P· C,PμCĤPjC-PSP°P»CHPSPsCĤ C†C,P°PrC-C" CĤ PSPēCĤPePsPIPsC— PSPμPrPsC†C,P°C,PSPsC†C,C- (PŸPŸPĶPĶ) PIPiP»PēPI PrC-P°P»C-P·C† PSP° P·P°PiP°P»CHPSPēPNē PeP»C-CĤPμPSC† C,PsC,,P°C†PēC,PēPSC-P±C† P±C†PI PIC-PrPSPsC†PSPs PSPμPIPμP»PēPePēPj. PμC-C†P»CĬ PsPrPSPsPeCĤP°C,PSPsPiPs P·P°C†C,PsC†C†PIP°PSPSCĬ PrPsP·Pē 10 PjPi C†PμCĤPμPrPSC" P·PSP°C†PμPSPSCĬ AUC C† PĪP°C†C-C" PSC,C-PI C-P· PŸPŸPĶPĶ, PIPēP·PSP°C†PμPSPμ PSP° PsC†PSPsPIC- PePsPSC†PμPSC,CĤP°C†C-PNē, PIPēPjC-CĤCĬPSPēC... C† PrPμPSCĤ P±PμP· PrC-P°P»C-P·C†, P±C†P»Ps PĪCĤPēP±P»PēP·PSPs PSP° 40 % (90 % P"†: 1,5BĤ"95 %) PIPëC‰PēPj PĪPsCĤC-PI PSCĬPSPs P· C,P°PePēPj C† PĪP°C†C-C" PSC,C-PI P· PSPsCĤPjP°P»CHPSPsCĤ C,,C†PSPeC†C-C" CĤ PSPēCĤPsPe. Pj PeP»C-PSC-C†PSPēC... PrPsC†P»C-PrP¶PμPSPSCĬC... C,PsC,,P°C†PēC,PēPSC-P± PSPμ PsC†C-PSCĤPIP°P»Pē PI PĪP°C†C-C" PSC,C-PI C-P· PIPëC...C-PrPSPēPj P·PSP°C†PμPSPSCĬPj PeP»C-CĤPμPSC†C† PeCĤPμP°C,PēPSC-PSC† (CĤPsP·CĤP°C...PsPIP°PSPēPj P·P° C,,PsCĤPjC†P»PsCĤ PĤPsPeCĤPsC,,C,P° BĤ" P"PsP»C,P°) PjPμPSC€Pμ 40 PjP»/C...PI (PrPēPI. CĤPsP·PrC-P» B«PŸPĪPsC†C-P± P·P°C†C,PsC†C†PIP°PSPSCĬ C,P° PrPsP·PēB»).

PμPμC†C-PSPePsPIP° PSPμPrPsC†C,P°C,PSC-C†C,CH

PJ PĭP°C†C-C" PSC, C-PI C-P· P»PμPĭPePsCĤ (PeP»P°CĬCř PĤ P·P° PeP»P°CĬPĕC,, C-PeP°C†C-C" CĤ PŠP°PNĕP»PrP° BĤ" PμBĤ™ CĤ) C,P° PĭPsPjC-CĤPSPsCĤ (PeP»P°CĬCř B P·P° PeP»P°CĬPĕC,, C-PeP°C†C-C" CĤ PŠP°PNĕP»PrP° BĤ" PμBĤ™ CĤ) PĭPμC†C-PSPePsPIPsCĤ PSPμPrPsCĬC,P°C,PSC-CĬC,CĤ P·PSP°C†PμPSPSCĬ AUC P·P±C-P»CHCĕCřPIP°P»PĕCĬCĬ PSP° 3 % C,P° 65 % PIC-PrPĭPsPIC-PrPSPs, PĭPsCĤC-PIPsCĬPSPs C-P· C,P°PePĕPjPĕ Cř PĭP°C†C-C" PSC, C-PI C-P· PSPsCĤPjP°P»CHPSPsCĤ C,,CřPSPeC†C-C" CĤ PĭPμC†C-PSPePĕ. PJ PeP»C-PSC-C†PSPĕC... PrPsCĬP»C-PrP¶PμPSPSCĬC... C,PsC,,P°C†PĕC,PĕPSC-P± PSPμ PsC†C-PSCĤPIP°P»Pĕ PI PĭP°C†C-C" PSC, C-PI C-P· C,CĬP¶PePsCĤ (PeP»P°CĬCř C P·P° PeP»P°CĬPĕC,, C-PeP°C†C-C" CĤ PŠP°PNĕP»PrP° BĤ" PμBĤ™ CĤ) PĭPμC†C-PSPePsPIPsCĤ PSPμPrPsCĬC,P°C,PSC-CĬC,CĤ (PrPĕPI. CĤPsP·PrC-P»Pĕ B«PŸPĭPsCĬC-P± P·P°CĬC,PsCĬCřPIP°PSPSCĬ C,P° PrPsP·PĕB» C,P° B«PhCĬPsP±P»PĕPIPsCĬC,C- P·P°CĬC,PsCĬCřPIP°PSPSCĬB») P°P±Ps PI PĭP°C†C-C" PSC, C-PI C-P· PĭPsP·PĕC,PĕPIPsPĕPj CĤPμP·CřP»CHC,P°C,PsPj C,PμCĬC,Cř PSP° PĭPμPĭP°C,PĕC, B P°P±Ps PĭPμPĭP°C,PĕC, C PĭC-Pr C†P°CĬ CĬPeCĤPĕPSC-PSPiCř.

P·P·P°C" PjPsPrC-C—

PŸPsC,,P°C†PĕC,PĕPSC-P± PSPμ C" C-PSPiC-P±C-C,PsCĤPsPj P°P±Ps C-PSPrCřPeC,PsCĤPsPj C-P·PsC,,PμCĤPjPμPSC, C-PI CĬPĕCĬC,PμPjPĕ CYP (CYP1A2, CYP2B6, CYP2C8, CYP2C9, CYP2C19, CYP2D6 C,P° CYP3A4) C- PSPμ C" C-PSPiC-P±C-C,PsCĤPsPj C-P·PsC,,PsCĤPj CřCĤPĕPrPĕPSPrPĕC,,PsCĬC,,P°C,BPiP»CĤPeCřCĤPsPSC-P»C,CĤP°PSCĬC,,PμCĤP°P·Pĕ (UGT) (UGT1A1, UGT1A4, UGT1A6, UGT1A9 C,P° UGT2B7). PŸPsC,,P°C†PĕC,PĕPSC-P± PSPμ C" C-PSPiC-P±C-C,PsCĤPsPj MDR1, OATP1B1/1B3, OCT2, OAT1/3 P°P±Ps P±C-P»PeP° PjPSPsP¶PĕPSPSPsC— P»C-PeP°CĤCĬCHPePsC— CĤPμP·PĕCĬC,PμPSC,PSPsCĬC,C- Cř PeP»C-PSC-C†PSPs P·PSP°C†CřC%PeC... PePsPSC†PμPSC,CĤP°C†C-CĬC....

PμP°C†C-C" PSC,Pĕ PrPĕC,CĬC†PsPiPs PIC-PeCř

PαP°CĤPjP°PePsPeC-PSPμC,PĕPeP° PI PrC-C,PμPNĕ P· CĤPIPμPSC-P»CHPSPĕPj C-PrC-PsPĭP°C,PĕC†PSPĕPj P°CĤC,CĤPĕC,PsPj

P"°PSC- PĭPsPĭCřP»CĬC†C-PNĕPSPsPiPs C,,P°CĤPjP°PePsPeC-PSPμC,PĕC†PSPsPiPs P°PSP°P»C-P·Cř, P·P°CĬPSPsPIP°PSPsPiPs PSP° CĤPμP·CřP»CHC,P°C,P°C... P·P°CĬC,PsCĬCřPIP°PSPSCĬ C,PsC,,P°C†PĕC,PĕPSC-P±Cř Cř C,,PsCĤPjC- C,P°P±P»PμC,PsPe, PĭPeCĤPĕC,PĕC... PĭP»C-PIPePsPIPsCĤ PsP±PsP»PsSPPePsCĤ, PĭPs 5 PjPi PrPIP° CĤP°P·Pĕ PSP° PrPsP±Cř PNĕ C,PsC,,P°C†PĕC,PĕPSC-P±Cř Cř C,,PsCĤPjC- CĤPsP·C†PĕPSCř PrP»CĬ PĭPμCĤPsCĤP°P»CHPSPsPiPs P·P°CĬC,PsCĬCřPIP°PSPSCĬ PI PμPePIC-PIP°P»PμPSC,PSC-PNĕ PrPsP·C-, CĤPsP·CĤP°C...PsPIP°PSC-PNĕ PSP° PsCĬPSPsPIC- PjP°CĬPĕ C,C-P»P°, PrPIP° CĤP°P·Pĕ PSP° PrPsP±Cř PĭPeP°P·CřCĤC,CH, C%Ps PI PĭP°C†C-C" PSC, C-PI P· P®P†PĤ PeP»C-CĤPμPSCĬ C,P° PsP±BĤ™ C" Pj CĤPsP·PĭPsPrC-P»Cř C,PsC,,P°C†PĕC,PĕPSC-P±Cř P·PjPμPSCĕCřCĤC,CHCĬCĬ P·C- P·PjPμPSCĕPμPSPSCĬPj PjP°CĬPĕ C,C-P»P°. PķP°CĬPIPsC- PrP°PSC- CĬPIC-PrC†P°C,CH PĭCĤPs PIC-PrCĬCřC,PSC-CĬC,CH PeP»C-PSC-C†PSPs P·PSP°C†CřC%PeC... PIC-PrPjC-PSPSPsCĬC,PμPNĕ PI PμPeCĬPĭPsP·PĕC†C-C— C,PsC,,P°C†PĕC,PĕPSC-P±Cř (AUC) P·P°P»PμP¶PSPs PIC-Pr PIC-PeCř, CĤP°CĬPsPIPsC— PĭCĤPĕPSP°P»PμP¶PSPsCĬC,C-, CĬC,P°C,C-, C,PĕPĭCř PĭP°C†C-C" PSC,P° P°P±Ps PĭPĕC...C-PrPSPsPiPs CĬC,CřPĭPμPSCĬ C,CĬP¶PePsCĬC,C- P·P°C...PIPsCĤCĤPIP°PSPSCĬ. PĤC-P¶C-PSPrPĕPIC-PrCřP°P»CHPSP° PIP°CĤC-P°P±PμP»CHPSC-CĬC,CH (PePsPμC,,C-C†C-C" PSC, PIP°CĤC-P°C†C-C—, %) PrP»CĬ P·PSP°C†PμPSCĤ (AUC) PsC†C-PSCĤPIP°P»P°CĬCĬ PĭCĤPĕP±P»PĕP·PSPs Cř 24 %.

РљР»С-РSC-С‡РSC- С...Р°СђР°РёС,РµСђРёСђС,РёРёРё.

РµРsРёР°Р°Р°РSPSCЦ.

Р РµРІРјР°С,РsС—РrРSPёРНё Р°СђС,СђРёС.

РђРsС,,Р°С‡РёС,РёРSC-Р± Сѓ РёРsРјР±С-РSP°С‡С-С— Р· РјРµС,РsС,СђРµРёСђР°С,РsРј (MTX)
РіРsРёР°Р°Р°РSPёРНё РrР»СЦ Р»С-РёСѓРІР°РSPSCЦ Р°РёС,РёРІРSPsРіРs
СђРµРІРјР°С,РsС—РrРSPsРіРs Р°СђС,СђРёС,Сѓ (Р Рђ) РіРsРјС-СђРSPsРіРs РNё С,СЦР¶Р¶РёРsРіРs
СђС,СѓРіРµРSCЦ РІ РrРsСђРsСђР»РёС... РіР°С‡С-С"РSC,С-РІ, СЦРёС- РјР°Р»РёС
РSPµРrРsСђС,Р°С,РSCђ РІС-РrРіРsРІС-РrСђ РSP° РsРrРёРs Р°Р±Рs РrРµС-Р»СђРёР°
РіСђРsС,РёСђРµРІРјР°С,РёС‡РSPёС... РіСђРµРіР°Р°СђР°С,С-РІ, С%Рs РјРsРrРёС,,С-РёСѓСђС,Сђ
РіРµСђРµР±С-Рі Р°Р°С...РІsСђСђРІР°РSPSCЦ (DMARD), Р°Р±Рs РІ СЦРёРёС...
СђРіРіРsСђС,РµСђС-РіР°С"С,СђСђСЦ РSPµРіРµСђРµРSPsСђРёС-СђС,Сђ С‡РёС...
РіСђРµРіР°Р°СђР°С,С-РІ. РђРsС,,Р°С‡РёС,РёРSC-Р± РјРsР¶РSP° РіСђРёР°РSP°С‡Р°С,Рё СЦРё
РјРsРSPsС,РµСђР°РіС-Сђ РІ СђР°Р°С- РSPµРіРµСђРµРSPsСђРёС-СђС,С- РTX Р°Р±Рs
РSPµРrРsС‡С-Р»СђРSPsСђС,С- Р»С-РёСѓРІР°РSPSCЦ РTX (РrРёРІ. СђРsР·РrС-Р»РёС
В«РђСђРsР±Р»РёРsСђС,С- Р°СђС,РsСђСѓРІР°РSPSCЦВ» С,Р° В«Р°Р°С"РјРsРrС-СЦ Р·
С-РSCёРёРјРё Р»С-РёР°СђСђСђРёРё Р°СђРsР±Р°РјРё С,Р° С-РSCёС- РІРёРrРёС
РІР°Р°С"РјРsРrС-РНёВ»).

РµСђРsСђС-Р°С,РёС‡РSPёРНё Р°СђС,СђРёС.

РђРsС,,Р°С‡РёС,РёРSC-Р± Сѓ РёРsРјР±С-РSP°С‡С-С— Р· РTX РіРsРёР°Р°Р°РSPёРНё РrР»СЦ
Р»С-РёСѓРІР°РSPSCЦ Р°РёС,РёРІРSPsРіРs РіСђРsСђС-Р°С,РёС‡РSPsРіРs Р°СђС,СђРёС,Сѓ
(РµСђРђ) Сѓ РrРsСђРsСђР»РёС... РіР°С‡С-С"РSC,С-РІ, СЦРёС- РјР°Р»РёС
РSPµРrРsСђС,Р°С,РSCђ РІС-РrРіРsРІС-РrСђ РSP° РіРsРіРµСђРµРrРSCђ С,РµСђР°РіС-Сђ
РіСђРsС,РёСђРµРІРјР°С,РёС‡РSPёРјРё РіСђРµРіР°Р°СђР°С,Р°РјРё, С%Рs
РјРsРrРёС,,С-РёСѓСђС,Сђ РіРµСђРµР±С-Рі Р°Р°С...РІsСђСђРІР°РSPSCЦ (DMARD), Р°Р±Рs
РSPµРіРµСђРµРSPsСђРёС-СђС,Сђ.

РђРSPёС-Р»РsР·СѓСђС‡РёРНё СђРіРіРsРSPrРёР»С-С.

РђРsС,,Р°С‡РёС,РёРSC-Р± РіРsРёР°Р°Р°РSPёРНё РrР»СЦ Р»С-РёСѓРІР°РSPSCЦ
РrРsСђРsСђР»РёС... РіР°С‡С-С"РSC,С-РІ С-Р· Р°РёС,РёРІРSPёРј Р°РSPёС-Р»РsР·СѓСђС‡РёРё
СђРіРіРsРSPrРёР»С-С,РsРј (РђРђ), Сѓ СЦРёРёС... РSPµ Р±СѓР»Р° РrРsСђСЦРіРіРSCѓС,Р°
РSP°Р»РµР¶РSP° РІС-РrРіРsРІС-РrСђ РSP° СђС,Р°РSPrР°СђС,РSCѓ С,РµСђР°РіС-Сђ.

Р°РёСђР°Р°РёРsРІРёРНё РёРsР»С-С.

РђРsС,,Р°С‡РёС,РёРSC-Р± РіРsРёР°Р°Р°РSPёРНё РrР»СЦ Р»С-РёСѓРІР°РSPSCЦ
РrРsСђРsСђР»РыС... РіР°С‡С-С"РSC,С-РІ Р· Р°РёС,РёРІРSPёРј РІРёСђР°Р°РёРsРІРё
РёРsР»С-С,РsРј (Р°Рђ) РіРsРјС-СђРSPsРіРs Р°Р±Рs С,СЦР¶Р¶РёРsРіРs СђС,СѓРіРµРSCЦ, Сѓ
СЦРёРёС... СђРіРіРsСђС,РµСђС-РіР°Р»Р°СђР°СђРµРSPµРrРsСђС,Р°С,РSCЦ РІС-РrРіРsРІС-РrСђ
РSP° СђС,Р°РSPrР°СђС,РSCѓ С,РµСђР°РіС-Сђ С‡РёС,РµСђР°РіС-Сђ
Р±С-РsР»РsРіС-С‡РSPёРјРё РіСђРµРіР°Р°СђР°С,Р°РјРё, РІС,СђР°С,Р° РІС-РrРіРsРІС-РrС- РSP°
Р»С-РёСѓРІР°РSPSCЦ С‡РёРјРё РіСђРµРіР°Р°СђР°С,Р°РјРы Р°Р±Рs С—С...
РSPµРіРµСђРµРSPsСђРёС-СђС,Сђ.

Р®РІРµРSC-Р»СђРSPёРНё С-РrС-РsРіР°С,РёС‡РSPёРНё Р°СђС,СђРёС, (Р®РђРђ)

РђРsС,,Р°С‡РёС,РёРSC-Р± РіРsРёР°Р°Р°РSPёРНё РrР»СЦ Р»С-РёСѓРІР°РSPSCЦ
Р°РёС,РёРІРSPsРіРs РіРsР»С-Р°СђС,РёРёСѓР»СЦСђРSPsРіРs СђРІРµРµС-Р»СђРSPsРіРs

C-PrC-PsP^oC, P^oC†PSPsPiPs P^oC₇C, C₇P^oC, C₇ (PiPsP»C-P^oC₇C, C₇P^oC, C₇ P·
PiPsP·P^oC, P^oPIPS^oPj [RF] P^oP±Ps PSPμPiP^oC, P^oPIPS^oPj [RF-] C₇PμP·C₇P»CHC, P^oC, PsPj
C, PμC₇C, C₇ PSP^o C₇PμPiPjP^oC, PsC—PrPSP^oPN₂ C,, P^oPeC, PsC₇ C- PiPsC₇P^oC₇PμPSPsPiPs
PsP»C-PiPsP^oC₇C, C₇P^oC, C₇) C₇ PiP^oC†C-C”PSC, C-PI PrP^oC, C₇C†PsPiPs PIC-PeC₇ P· PjP^oC₇PsC₇
C, C-P»P^o ≥ 40 PePi, C₇PeC- PjP^oP»P^o PSPμPrPsC₇C, P^oC, PSC₇ PIC-PrPiPsPIC-PrCH PSP^o
PiPsPiPμC₇PμPrPSC₇ C, PμC₇P^oPiC-C₇ DMARD.

P^oPsC,, P^oC†P^oC, P^oPSC-P± PjPsP^oPIPS^o P·P^oC₇C, PsC₇PsPIC₇PIP^oC, P^o PI PePsPjP±C-PSP^oC†C-C—
P· P^oP^oPI P^oP±Ps C₇Pe PjPsPSPsC, PμC₇P^oPiC-C₇ PI C₇P^oP·C-
PSPμPiPμC₇PμPSPsC₇P^oPjPsC₇C, C- P^oP^oPI P^oP±Ps C₇PeC%Ps PiC₇PsPrPsPIP^oPIPS^oPSC₇
P·P^oC₇C, PsC₇C₇PIP^oPSPSC₇ P^oP^oPI P^oP±Ps C₇PeC%Ps PiC₇PsPrPsPIP^oPIPS^oPSC₇

PμC₇PsC, P^oPiPsPeP^oP·P^oPSPSC₇.

P“C-PiPμC₇C†C₇C, P»P^oPIC-C₇C, CH PrPs PrC-C₇C†PsC— C₇PμC†PsPIP^oPSP^o P^oP±Ps
P±C₇PrCH-C₇PePsC— P· PrPsPiPsPjC-P^oPIPS^oPjC... C₇PμC†PsPIP^oPS PiC₇PμPiP^oC₇P^oC, C₇,
P·P^oP·PSP^oC†PμPSP^oC... C₇ C₇PsP·PrC-P»C- B«P^oPeP»P^oPrB».

P^oPeC, P^oPIPS^o C,, PsC₇PjP^o C, C₇P±PμC₇PeC₇P»CHPsP·C₇ (P^oP’), C₇PμC₇PN₂PsP·PSC-
C-PSC,, PμPeC†C-C—, C, P^oPeC- C₇Pe C₇PμPiC₇P^oC₇, P^oP±Ps PsPiPsC₇C, C₇PSC-C₇C, P^oC†PSC-
C-PSC,, PμPeC†C-C— (PrP^oPI. C₇PsP·PrC-P» B«P^oC₇PsP±P»P^oPIPsC₇C, C-
P·P^oC₇C, PsC₇C₇PIP^oPSPSC₇IB»).

P^oC₇PeP^o PiPμC†C-PSPePsPIP^o PSPμPrPsC₇C, P^oC, PSC-C₇C, CH (PrP^oPI. C₇PsP·PrC-P»
B«P^oPIPsC₇C-P± P·P^oC₇C, PsC₇C₇PIP^oPSPSC₇ C, P^o PrPsP·P^oB»).

P^oP^oPiC-C, PSC-C₇C, CH C- P»P^oPeC, P^oC†C-C₇ (PrP^oPI. C₇PsP·PrC-P»
B«P—P^oC₇C, PsC₇C₇PIP^oPSPSC₇ C₇ PiPμC₇C-PsPr PIP^oPiC-C, PSPsC₇C, C- P^oP±Ps
PiPsPrC₇PIP^oPSPSC₇ PiC₇C₇PrPrCHB»).

P’P·P^oC”PjPsPrC-C₇ P· C-PSC₇PePjP^o P»C-PeP^oC₇C₇CHPeP^oPjP^o P·P^oC₇PsP±P^oPjP^o C, P^o C-PSC₇C- PIP^oPrP^o PIP·P^oC”PjPsPrC-PN₂.

PμPsC, PμPSC†C-PN₂PSP^o P·PrP^oC, PSC-C₇C, CH C-PSC₇PeC... P»C-PeP^oC₇C₇CHPeP^oC...
P·P^oC₇PsP±C-PI PIP^oP»P^oPIP^oC, P^o PSP^o C,, P^oC₇PjP^oPePsPeC-PSPμC, P^oPeC₇ (PαP₇)
C, PsC,, P^oC†P^oC, P^oPSC-P±C₇

P^oC₇PeC-P»CHPeP^o C, PsC,, P^oC†P^oC, P^oPSC-P± PjPμC, P^oP±PsP»C-P·C₇C”C, CHC₇C₇
C-P·PsC,, PμC₇PjPμPSC, PsPj CYP3A4, C-PjPsPIC-C₇PSPμ PIP^oPSP^oPePSPμPSPSC₇
PIP·P^oC”PjPsPrC-PN₂ C-P· P»C-PeP^oC₇C₇CHPeP^oPjP^o P·P^oC₇PsP±P^oPjP^o, C₇PeC-
PiC₇P^oPIPSC-C†C₇C, CH P^oP±Ps C-PSP^oC₇PeC₇C, CH CYP3A4. P·PeC₇PiPsP·P^oC†C-C₇
C, PsC,, P^oC†P^oC, P^oPSC-P±C₇ P·P±C-P»CHC₇C₇C”C, CHC₇C₇ PI C₇P^oP·C-
PsPrPSPsC†P^oC₇PSPsPiPs P·P^oC₇C, PsC₇C₇PIP^oPSPSC₇ P· PiPsC, C₇P^oPIPS^oPjP^o
C-PSPiC-P±C-C, PsC₇P^oPjP^o CYP3A4 (PSP^oPiC₇P^oPeP»P^oPr, PePμC, PsPePsPSP^oP·PsP»PsPj)
P^oP±Ps PePsP»P^o PsPrPSPsC†P^oC₇PSPμ P·P^oC₇C, PsC₇C₇PIP^oPSPSC₇ PsPrPSPsPiPs C†P^o
PrPμPeC-P»CHPePsC... P»C-PeP^oC₇C₇CHPeP^oC... P·P^oC₇PsP±C-PI (PSP^oPiC₇P^oPeP»P^oPr,
C,, P»C₇PePsPSP^oP·PsP»C₇) PiC₇P^oPIPsPrP^oC, CH C₇Pe PrPs PiPsPjC-C₇PSPsPiPs
PiC₇P^oPIPSC-C†PμPSPSC₇ CYP3A4, C, P^oPe C- PrPs PiPsC, C₇P^oPIPS^oPiPs
PiC₇P^oPIPSC-C†PμPSPSC₇ CYP2C19 (PrP^oPI. C₇PsP·PrC-P» B«P^oPIPsC₇C-P±

P·P°CfC,PsCfCfPIP°PSPSCf C,P° PrPsP·PëB»).

P·PeCfPpPsP·PëCfC-Cl C,PsC,,P°CfPëC,PëPSC-P±Cf P·PjPµPSCfCfC”C,CHCfCfCl PI CḡP°P·C-
PsPrPSPScfP°CfPSPsPiPs P·P°CfC,PsCfCfPIP°PSPSCf P· PpPsC,CfP¶PSPëPjPë
C-PSPrCfPeC,PsCḡP°PjPë C-P·PsC,,PµCḡPjPµPSC,C-PI CfPëCfC,PµPjPë CYP
(PSP°PpCḡPëPeP»P°Pr, CḡPëC,,P°PjPpC-CfPëPSPsPj). PḡP°P»PsPMpPjPsPIC-CḡPSPs, C%Ps
C-PSPiC-P±C-C,PsCḡPë CYP2C19 PsPeCḡPµPjPs P°P±Ps P -PiP»C-PePsPpCḡPsC,PµC—PSCf
C-CfC,PsC,PSPs P·PjC-PSCḡPIP°C,PëPjCfC,CH PḡPḡ C,PsC,,P°CfPëC,PëPSC-P±Cf.

PḡPrPSPScfP°CfPSPµ P·P°CfC,PsCfCfPIP°PSPSCf P· PePµC,PsPePsPSP°P·PsP»PsPj
(PpPsC,CfP¶PSPëPj C-PSPiC-P±C-C,PsCḡPsPj CYP3A4), C,,P»CfPePsPSP°P·PsP»PsPj
(PpPsPjC-CḡPSPëPj C-PSPiC-P±C-C,PsCḡPsPj CYP3A4 C- PpPsC,CfP¶PSPëPj
C-PSPiC-P±C-C,PsCḡPsPj CYP2C19), C,P°PeCḡPsP»C-PjCfCfPsPj (PpPsPjC-CḡPSPëPj
C-PSPiC-P±C-C,PsCḡPsPj CYP3A4) C- CfPëPeP»PsCfPpPsCḡPëPSPsPj (PpPsPjC-CḡPSPëPj
C-PSPiC-P±C-C,PsCḡPsPj CYP3A4) PpC-PrPIPëC%CfPIP°P»Ps P·PSP°CfPµPSPSCf AUC
C,PsC,,P°CfPëC,PëPSC-P±Cf, C,PsPrC- ClPe CḡPëC,,P°PjPpC-CfPëPS (PpPsC,CfP¶PSPëPḡ
C-PSPrCfPeC,PsCḡ C-P·PsC,,PµCḡPjPµPSC,C-PI CfPëCfC,PµPjPë CYP) P·PSPëP¶CfPIP°PI
P·PSP°CfPµPSPSCf AUC C,PsC,,P°CfPëC,PëPSC-P±Cf. PḡPrPSPScfP°CfPSPµ
P·P°CfC,PsCfCfPIP°PSPSCf C,PsC,,P°CfPëC,PëPSC-P±Cf P· PpPsC,CfP¶PSPëPjPë
C-PSPrCfPeC,PsCḡP°PjPë C-P·PsC,,PµCḡPjPµPSC,C-PI CfPëCfC,PµPjPë CYP
(PSP°PpCḡPëPeP»P°Pr, CḡPëC,,P°PjPpC-CfPëPSPsPj) PjPsP¶Pµ PpCḡPëP·PIPµCfC,Pë PrPs
PIC,CḡP°C,Pë P°P±Ps P·PSPëP¶PµPSPSCf PeP»C-PSC-CfPSPsC— PIC-PrPpPsPIC-PrC-.
PḡPrPSPScfP°CfPSPµ P·P°CfC,PsCfCfPIP°PSPSCf PpPsC,CfP¶PSPëC... C-PSPrCfPeC,PsCḡC-PI
CYP3A4 P· C,PsC,,P°CfPëC,PëPSC-P±PsPj PSPµ CḡPµPePsPjPµPSPrCfC”C,CHCfCfCl.
PḡPrPSPScfP°CfPSPµ P·P°CfC,PsCfCfPIP°PSPSCf P· PePµC,PsPePsPSP°P·PsP»PsPj C-
C,,P»CfPePsPSP°P·PsP»PsPj PpCḡPëP·PIPsPrPëP»Ps PrPs PpC-PrPIPëC%PµPSPSCf
P·PSP°CfPµPSCḡ C_{max} C,PsC,,P°CfPëC,PëPSC-P±Cf, C,PsPrC- ClPe C,P°PeCḡPsP»C-PjCfCf,
CfPëPeP»PsCfPpPsCḡPëPS C- CḡPëC,,P°PjPpC-CfPëPS P·PSPëP¶CfPIP°P»Pë P·PSP°CfPµPSPSCf
C_{max} C,PsC,,P°CfPëC,PëPSC-P±Cf. PḡPrPSPScfP°CfPSPµ P·P°CfC,PsCfCfPIP°PSPSCf P· MTX Cf
PrPsP·C- 15ḡḡ”25 PjPi PsPrPëPS CḡP°P· PSP° C,PëP¶PrPµPSCḡ PSPµ PIPp»PëPIP°P»Ps PSP°
PḡPḡ C,PsC,,P°CfPëC,PëPSC-P±Cf PI PpP°CfC-C”PSC,C-PI C-P· P Pḡ (PrPëPI. CḡPëCfCfPSPsPe
1).

P PëCfCfPSPsPe 1. P’PpP»PëPI C-PSCfPëC... P»C-PeP°CḡCfCHPePëC... P·P°CfPsP±C-PI PSP°
C,,P°CḡPjP°PePsPeC-PSPµC,PëPeCf C,PsC,,P°CfPëC,PëPSC-P±Cf

0
0,5
1
1,5
2
2,5
Cmax
AUC
Cmax
AUC
Cmax
AUC

Cmax
AUC
Cmax
AUC
Cmax
AUC

P†PSPiC-P±C-C,PsCᄡ CYP3A
PᄡPᄢC,PsPePsPSP°P·PsP»
P†PSPiC-P±C-C,PsCᄡ CYP3A C,P° CYP2C19
PᄡP»C†PePsPSP°P·PsP»
P†PSPrCžPeC,PsCᄡ CYP
P PëC,,P°PjPiC-C†PëPS
PᄡPᄢC,PsC,CᄡPᄢPeC†P°C,
PŸP°PeCᄡPsP»C-PjC†C†
P†PëPeP»PsC†PiPsCᄡPëPS
P°PSP·C† C,PsC,,P°C†PëC,PëPSC-P±C† C†P»C-Pr P·PjPᄢPSC€PëC,Pë P°

P°PSP·C† C,PsC,,P°C†PëC,PëPSC-P±C† C†P»C-Pr P·PjPᄢPSC€PëC,Pë P°

P·C,,PᄢPeC,PëPIPSC-C†C,CH PjPsPᄡPᄢ P·PSPëP·PëC,PëC†Cᄡ
PᄡPsCᄡPëPiC†PIP°PSPSCᄡ PrPsP·Pë PSPᄢ PiPsC,CᄡC-P±PSPᄢ
PᄡPrPSPsC†P°C†PSPsPiPs P·P°C†C,PsC†C†PIP°PSPSCᄡ C,PsC,,P°C†PëC,PëPSC-P±C†
P·C,P°PeCᄡPsP»C-PjC†C†PsPj C†P»C-Pr C†PSPëPeP°C,Pë
PᄡPrPSPsC†P°C†PSPsPiPs P·P°C†C,PsC†C†PIP°PSPSCᄡ C,PsC,,P°C†PëC,PëPSC-P±C†

P·C†PëPeP»PsC†PiPsCᄡPëPSPsPj C†P»C-Pr C†PSPëPeP°C,Pë
P°C-PrPSPsC€PᄢPSPSCᄡ C†C,PsC†PsPIPSPs PePsPSC,CᄡPsP»CHPSPsC— PiCᄡC†PiPë
PŸC†PiC†C,PSC-PNᄡ
P»C-PeP°CᄡC†CHPePëPNᄡ P·P°C†C-P±
PᄡPᄡ
P°C-PrPSPsC€PᄢPSPSCᄡ C,P° 90%-PNᄡ P°P†
P PᄢPePsPjPᄢPSPrP°C†C-C—

PᄢCᄡPëPjC-C,PeP°: PᄢC-Pr PePsPSC,CᄡPsP»CHPSPsCᄡ PiCᄡC†PiPsCᄡ PjP°CᄡC,CHC†Cᄡ PSP°
C†PIP°P·C- PiP°C†C-C°PSC,Pë, CᄡPeC- PsC,CᄡPëPjC†PIP°P»Pë P»PëC€Pᄢ
C,PsC,,P°C†PëC,PëPSC-P±.

B· P°B P°PSP·C† C,PsC,,P°C†PëC,PëPSC-P±C† C†P»C-Pr P·PjPᄢPSC€PëC,Pë PrPs 5 PjPi PrPIP°
CᄡP°P·Pë PSP° PrPsP±C† PiP°C†C-C°PSC,P°Pj, CᄡPeC- PsC,CᄡPëPjC†PIP°P»Pë PrPsP·C† 10 PjPi
PrPIP° CᄡP°P·Pë PSP° PrPsP±C†. P°PSP·C† C,PsC,,P°C†PëC,PëPSC-P±C† C†P»C-Pr
P·PjPᄢPSC€PëC,Pë PrPs 5 PjPi PsPrPëPS CᄡP°P· PSP° PrPsP±C† PiP°C†C-C°PSC,P°Pj, CᄡPeC-
PsC,CᄡPëPjC†PIP°P»Pë PrPsP·C† 5 PjPi PrPIP° CᄡP°P·Pë PSP° PrPsP±C† (PrPëPI.
CᄡPsP·PrC-P» B«PŸPiPsC†C-P± P·P°C†C,PsC†C†PIP°PSPSCᄡ C,P° PrPsP·PëB»).

-

PᄢPsC,PᄢPSC†C-PNᄡPSP° P·PrP°C,PSC-C†C,CH C,PsC,,P°C†PëC,PëPSC-P±C† PIPiP»PëPIP°C,Pë
PSP° PᄡPᄡ C-PSC€PëC... P»C-PeP°CᄡC†CHPePëC... P·P°C†PsP±C-PI

PᄡPrPSPsC†P°C†PSPᄢ P·P°C†C,PsC†C†PIP°PSPSCᄡ C,PsC,,P°C†PëC,PëPSC-P±C† PSPᄢ
PIPiP»PëPIP°P»Ps PSP° PᄡPᄡ PiPᄢCᄡPsCᄡP°P»CHPSPëC... PePsPSC,CᄡP°C†PᄢPiC,PëPIC-PI Bᄡ“
P»PᄢPIPSPSPsCᄡPiPᄢC†C,CᄡPᄢP»C† PNᄡ PᄢC,PëPSC-P»PᄢC†C,CᄡP°PrC-PsP»C† Bᄡ“ C†
P·PrPsCᄡPsPIPëC... PᄡC-PSPsPe-PrPsP±CᄡPsPIPsP»CHC†C-PI.

Pj PiP°C†C-C°PSC,C-PI C-P· P Pᄡ PsPrPSPsC†P°C†PSPᄢ P·P°C†C,PsC†C†PIP°PSPSCᄡ

C,PsC,,P°C†PëC,PëPSC-P±Cř P· PҺPÿPГ Cř PrPsP·C- 15БҢ“25 PjPi PsPrPëPS CҢP°P· PSP°
C,PëPҢPrPμPSCҺ P·PSPëPҢCřPIP°P»Ps P·PSP°C‡PμPSPSCҢ AUC C- C_{max} PҺPÿPГ PSP° 10 C- 13 %
PIC-PrPіPsPIC-PrPSPs. PҮC,CřPіC-PSCҺ P·PSPëPҢPμPSPSCҢ PμPëCГPіPsP·PëC†C-C— PҺPÿPГ
PSPμ PIPëPjP°PiP°C” P·PjC-PSPë C-PSPPrPëPIC-PrCřP°P»CHbPSPs PiC-PrC-P±CҢP°PSPsC—
PrPsP·Pë PҺPÿPГ.

PμP°C†C-C”PSC,Pë PrPëC,CҢC‡PsPiPs PIC-PëCř

P”PsCГP»C-PrPҢPμPSPSCҢ PIP·P°C”PjPsPrC-C— P»C-PëP°CҢCГCHbPePëC... P·P°CГPsP±C-PI
PіCҢPsPiPsPrPëP»PëCГCҢ P»PëCëPμ P·P° CřC‡P°CГC,CҢ PrPsCҢPsCГP»PëC...
PіP°C†C-C”PSC,C-PI.

PҺCГPsP±P»PëPIPsCГC,C- P·P°CГC,PsCГCзPIP°PSPSCҢ.

PμPμCҢPμP»C-C‡PμPSPëPj PSPëPҢC‡Pμ PiCҢCřPіP°Pj PіP°C†C-C”PSC,C-PI
C,PsC,,P°C†PëC,PëPSC-P± CГP»C-Pr P·P°CГC,PsCГPsPICřPIP°C,Pë P»PëCëPμ P·P°
PIC-PrCГCřC,PSPsCГC,C- PIC-PrPіPsPIC-PrPSPëC... P°P»CHbC,PμCҢPSP°C,PëPIPsPëC...
PjPμC,PsPrC-PI P»C-PëCřPIP°PSPSCҢ:

- PіP°C†C-C”PSC,Pë PIC-PëPsPj 65 CҢPsPeC-PI C- CГC,P°CҢCëPμ;

- PіP°C†C-C”PSC,Pë P· P°C,PμCҢPsCГPeP»PμCҢPsC,PëC‡PSPëPjPë CГPμCҢC†PμPiPs-
CГCřPrPëPSPSPëPjPë P·P°C...PIPsCҢCHPIP°PSPSCҢPjPë PI P°PSP°PjPSPμP·C- P°P±Ps
C-PSCëPëPjPë C,,P°PeC,PsCҢP°PjPë CҢPëP·PëPeCř CГPμCҢC†PμPiPs-CГCřPrPëPSPSPëC...
P·P°C...PIPsCҢCHPIP°PSCҺ (PSP°PiCҢPëPeP»P°Pr, PeCřCҢC-PSPSCҢ PSP° PrP°PSPëPNë C‡P°CГ
C‡Pë PeCřCҢC-PSPSCҢ PiCҢPsC,CҢPiPsPj C,CҢPëPIP°P»PsPiPs C‡P°CГCř PI P°PSP°PjPSPμP·C-);

- PіP°C†C-C”PSC,Pë P· C,,P°PeC,PsCҢP°PjPë CҢPëP·PëPeCř CҢPsP·PIPëC,PeCř
P·P»PsCҢPeC-CГPSPëC... PSPsPiPsCřC,PIPsCҢPμPSCҺ (PSP°PiCҢPëPeP»P°Pr,
PSP°CҢPIPSC-CГC,CH P·P»PsCҢPeC-CГPSPsPiPs PSPsPiPsCřC,PIPsCҢPμPSPSCҢ PSP°
PrP°PSPëPNë C‡P°CГ C‡Pë PI P°PSP°PjPSPμP·C-).

P—P°CГC,PsCГCřPIP°PSPSCҢ PіP°C†C-C”PSC,P°Pj PIC-PëPsPj 65 CҢPsPeC-PI C- CГC,P°CҢCëPμ

P’CҢP°C...PsPICřCҢC‡Pë PiC-PrPIPëC%PμPSPëPNë CҢPëP·PëPe PIPëPSPëPePSPμPSPSCҢ
CГPμCҢPNëPsP·PSPëC... C-PSC,,PμPeC†C-PNë, C-PSC,,P°CҢPeC,Cř PjC-PsPeP°CҢPrP°,
P·P»PsCҢPeC-CГPSPëC... PSPsPiPsCřC,PIPsCҢPμPSCҺ C- CГPjPμCҢC,C- P· P±CřPrCHb-
CҢPePsC— PiCҢPëC‡PëPSPë Cř CҢP°P·C- P·P°CГC,PsCГCřPIP°PSPSCҢ
C,PsC,,P°C†PëC,PëPSC-P±Cř PіP°C†C-C”PSC,P°Pj PIC-PëPsPj 65 CҢPsPeC-PI C- CГC,P°CҢCëPμ,
C,PsC,,P°C†PëC,PëPSC-P± CГP»C-Pr P·P°CГC,PsCГPsPICřPIP°C,Pë C,P°PePëPj
PіP°C†C-C”PSC,P°Pj P»PëCëPμ P·P° PIC-PrCГCřC,PSPsCГC,C- PIC-PrPіPsPIC-PrPSPëC...
P°P»CHbC,PμCҢPSP°C,PëPIPsPëC... PjPμC,PsPrC-PI P»C-PëCřPIP°PSPSCҢ (PrPëPI.
PrPsPrP°C,PePsPICř C-PSC,,PsCҢPjP°C†C-CҢ PSPëPҢC‡Pμ).

P—P°CГC,PsCГCřPIP°PSPSCҢ PI PePsPjP±C-PSP°C†C-C— P· C-PSCëPëPjPë
P»C-PëP°CҢCГCHbPePëPjPë P·P°CГPsP±P°PjPë

P—P°CГC,PsCГCřPIP°PSPSCҢ C,PsC,,P°C†PëC,PëPSC-P±Cř PI PePsPjP±C-PSP°C†C-C— P·
P±C-PsP»PsPiC-C‡PSPëPjPë PiCҢPμPіP°CҢP°C,P°PjPë, C,P°PePëPjPë CҢPe
P°PSC,P°PiPsPSC-CГC,Pë C,,P°PeC,PsCҢP° PSPμPeCҢPsP·Cř PiCřC...P»PëPSPë (PαPќPμ),
P°PSC,P°PiPsPSC-CГC,Pë C-PSC,PμCҢP»PμPNëPeC-PSCř (IL)-1R, P°PSC,P°PiPsPSC-CГC,Pë IL-6R,

PjPsPSPsPeP»PsPSP°P»CHbPSC- P°PSC,PëC,C-P»P° PrPs CD20, P°PSC,P°PiPsPSC-CfC,Pë IL-17, P°PSC,P°PiPsPSC-CfC,Pë IL-12/IL-23, P°PSC,PëC-PSC,PµPiCtjPëPSPë, CfPµP»PµPeC,PëPIPSC- PjPsPrCfP»CfC,PscTjPë PePsCfC,PëPjCfP»CfC†C-C— C,P° PiPsC,CfP¶PSC- C-PjCfPSPsPrPµPiCtjPµCfP°PSC,Pë, C,P°PeC- C¶Pe P°P·P°C,C-PsPiCtjPëPS, 6- PjPµCtjPeP°PiC,PsPiCfCtjPëPS, C†PëPeP»PsCfPiPsCtjPëPS C- C,P°PeCtjPsP»C-PjCfCf, PSPµ PIPëPIC†P°P»PsCfC¶, C,PsPjCf CfP»C-Pr CfPSPëPeP°C,Pë C,P°PePëC... PePsPjP±C-PSP°C†C-PNë Cf P·PIbTj™ C¶P·PeCf P· PjPsP¶P»PëPIC-CfC,Ct PiPsCfPëP»PµPSPSC¶ C-PjCfPSPsCfCfPiCtjPµCfC-C— C,P° PiC-PrPIPëC%oPµPSPëPj CtjPëP·PëPePsPj CtjPsP·PIPëC,PeCf C-PSC,,PµPeC†C-PNë.

PJ PeP»C-PSC-C†PSPëC... PrPsCfP»C-PrP¶PµPSPSC¶C... C%oPsPrPs PiPsPeP°P·P°PSPSC¶ P Pj CfPiPsCfC,PµCtjC-PiP°P»P°CfC¶ P±C-P»CHbC¶ PIPëCfPsPeP° C†P°CfC,Psc,P° PIPëPSPëPePSPµPSPSC¶ PiPsP±C-C†PSPëC... CtjPµP°PeC†C-PNë PiCtjPë P·P°CfC,PscCfCfPIP°PSPSC- PePsPjP±C-PSP°C†C-C— C,Psc,,P°C†PëC,PëPSC-P±Cf P· MTX PiPsCtjC-PIPSC¶PSPs P· PjPsPSPsC,PµCtjP°PiC-C”Ct C,Psc,,P°C†PëC,PëPSC-P±PsPj.

P—P°CfC,PscCfCfPIP°PSPSC¶ C,Psc,,P°C†PëC,PëPSC-P±Cf PI PePsPjP±C-PSP°C†C-C— P· C-PSPiC-P±C-C,PscTjP°PjPë C,,PsCfC,,PsPrC-PµCfC,PµCtjP°P·Pë 4 PSPµ PIPëPIC†P°P»PsCfC¶ PI PeP»C-PSC-C†PSPëC... PrPsCfP»C-PrP¶PµPSPSC¶C... C-P· P·P°CfC,PscCfCfPIP°PSPSC¶Pj C,Psc,,P°C†PëC,PëPSC-P±Cf.

P’PµPSPsP·PSP° C,CtjPsPjP±PsPµPjP±PsP»C-C¶ (P’PÿP·)

PJ PiP°C†C-C”PSC,C-PI, C¶PeC- PsC,CtjPëPjCfPIP°P»Pë C,Psc,,P°C†PëC,PëPSC-P±, CfPiPsCfC,PµCtjC-PiP°P»PëCfC¶ CfPµCtjPNëPsP·PSC- CfCfPeP»P°PrPSPµPSPSC¶ Cf PIPëPiP»C¶PrC- P’PÿP·, PIPëP»CtC†PSPs P· C,CtjPsPjP±PsPµPjP±PsP»C-C”Ct P»PµPiPµPSPµPIPsC— P°CtjC,PµCtjC-C— (PÿP·P·Pj), PrPµC¶PeC- P· PIPëPiP°PrPeC-PI P±CfP»Pë P»PµC,P°P»CHbPSPëPjPë, C- C,CtjPsPjP±PsP·Cf PiP»PëP±PsPePëC... PIPµPS (PÿP”P’). PJ CtjP°PSPrPsPjC-P·PsPIP°PSPsPjCf PiC-CfP»C¶CtjPµC”CfC,CtjP°C†C-PNëPSPsPjCf PrPsCfP»C-PrP¶PµPSPSC- P±PµP·PiPµPePë P·P° CfC†P°CfC,Ct PiP°C†C-C”PSC,C-PI C-P· CtjPµPIPjP°C,Psc—PrPSPëPj P°CtjC,CtjPëC,PsPj PIC-PePsPj PIC-Pr 50 CtjPsPeC-PI P· PiCtjPëPSP°PNëPjPSC- PsPrPSPëPj PrPsPrP°C,PePsPIPëPj C,,P°PeC,PscTjPsPj CtjPëP·PëPeCf CfPµCtjC†PµPIPs-CfCfPrPëPSPSPëC... CfCfPeP»P°PrPSPµPSCb CfPiPsCfC,PµCtjC-PiP°PICfC¶ PrPsP·PsP·P°P»PµP¶PSPëPNë PiC-PrPIPëC%oPµPSPëPNë CtjPëP·PëPe CtjPsP·PIPëC,PeCf P’PÿP· PiC-Pr C†P°Cf P·P°CfC,PscCfCfPIP°PSPSC¶ C,Psc,,P°C†PëC,PëPSC-P±Cf PiPsCtjC-PIPSC¶PSPs P· C-PSPiC-P±C-C,PscTjP°PjPë PαPκPµ (PrPëPI. CtjPsP·PrC-P»Pë B«PµPsP±C-C†PSC- CtjPµP°PeC†C-C—B» C,P° B«PαP°CtjPjP°PePsP»PsPiC-C†PSC- PIP»P°CfC,PëPIPsCfC,C-B»).

PJ PiPsC€CfPePsPIPsPjCf CtjPµC,CtjPsCfPiPµPeC,PëPIPSPsPjCf P°PSP°P»C-P·C- PI PjPµP¶P°C... C†CHbPsPiPs PrPsCfP»C-PrP¶PµPSPSC¶, PiCtjPsPIPµPrPµPSPsPjCf P·P° CfC†P°CfC,Ct PiP°C†C-C”PSC,C-PI C-P· PIC-PrPsPjPëPjPë C,,P°PeC,PscTjP°PjPë CtjPëP·PëPeCf P’PÿP·, PIPëPiP°PrPePë PSP°CfC,P°PSPSC¶ P’PÿP· PI PiPsPrP°P»CHbC€PsPjCf CfPiPsCfC,PµCtjC-PiP°P»PëCfC¶ C†P°CfC,C-C€Pµ PI PiP°C†C-C”PSC,C-PI, C¶PeC- PsC,CtjPëPjCfPIP°P»Pë C,Psc,,P°C†PëC,PëPSC-P± C- PI C¶PePëC... C†PµCtjPµP· 12 PjC-CfC¶C†C-PI C,PµCtjP°PiC-C— CtjC-PIPµPSCb D-PrPëPjPµCtjP° P±CfPI Cf PrPIP° CtjP°P·Pë PIPëC%oPµ PIPµCtjC...PSCbPsC— PjPµP¶C- PSPsCtjPjPë (≥ 2 × P’PµPκ), PiPsCtjC-PIPSC¶PSPs P· PiP°C†C-C”PSC,P°PjPë P· CtjC-PIPSPµPj D-PrPëPjPµCtjP° < 2 × P’PµPκ; C†C¶ C,PµPSPrPµPSC†C-C¶ PSPµ CfPiPsCfC,PµCtjC-PiP°P»P°CfCb Cf PiP°C†C-C”PSC,C-PI, C¶PeC- PsC,CtjPëPjCfPIP°P»Pë C-PSPiC-P±C-C,PscTjPë PαPκPµ. P†PSC,PµCtjPiCtjPµC,P°C†C-C¶ PsP±PjPµP¶CfC”C,CHbCfC¶ PSPëP·CHbPePsCt PeC-P»CHbPeC-CfC,Ct PiPsPrC-PNë P’PÿP· C,P° PsP±PjPµP¶PµPSPëPjPë CtjPµP·CfP»CHbC,P°C,P°PjPë P°PSP°P»C-P·C-PI PSP° D-PrPëPjPµCtj (C¶PePëPNë PsC†C-PSCtjPIP°PICfC¶ P»PëC€Pµ PSP° PIPëC...C-PrPSPsPjCf CtjC-PIPSC-,

C#PμCḡPμP· 12 PjC-CÍCḡC†C-PI C- PSP°PīCḡPēPeC-PSC†C- PrPsCÍP»C-PrP¶PμPSPSCḡ). Pj PīP°C†C-C"PS C,PI, CḡPeC- PSPμ PjP°P»Pē P'PŷP· PīC-Pr C#P°CÍ PrPsCÍP»C-PrP¶PμPSPSCḡ, CÍPμCḡPμPrPSC- CḡC-PIPSC- D-PrPēPjPμCḡP° P±CŕP»Pē P·PSP°C#CŕC%Ps P·PSPēP¶PμPSC- PSP° 12-PjCŕ PjC-CÍCḡC†C- PīPsCḡC-PIPSCḡPSPs P· PIPēC...C-PrPSPēPj CḡC-PIPSPμPj Cŕ PICÍC-C... PīCḡCŕPīP°C... C,PμCḡP°PīC-C—. PhPrPSP°Pe CḡC-PIPSC- D-PrPēPjPμCḡP° $\geq 2 \times P'P_{\text{H}}K_{\text{P}} \text{ PSP}^\circ 12\text{-PjCŕ PjC-CÍCḡC†C- CÍPīPsCÍC,PμCḡC-PiP°P} \gg \text{PēCÍCḡ}$ PīCḡPēP±P»PēP·PSPs PI 30 % PīP°C†C-C"PS C,PI P±PμP· PīPsPrP°P»CHC€PēC... PīPsPrC-PNē P'PŷP·, C%Ps PIPeP°P·CŕC" PSP° PsP±PjPμP¶PμPSCŕ CÍPīPμC†PēC,,C-C#PSC-CÍC,CH P°PSP°P»C-P·Cŕ PSP° D-PrPēPjPμCḡ Cŕ C†CHPsPjCŕ PrPsCÍP»C-PrP¶PμPSPSC-.

PŷPsC,,P°C†PēC,PēPSC-P± Cŕ PrPsP·C- 10 PjPi PrPIP° CḡP°P·Pē PSP° PrPsP±Cŕ PrP»Cḡ PīC-PrC,CḡPēPjCŕPīP°P»CHPSPsC— C,PμCḡP°PīC-C— PSPμ CḡPμPePsPjPμPSPŕCŕC"C,CHCÍCḡ P·P°CÍC,PsCÍPsPICŕPīP°C,Pē PīP°C†C-C"PS C,P°Pj C-P· P'P_{\text{H}}, Cŕ CḡPePēC... C" PIC-PrPsPjC- C,,P°PeC,PsCḡPē CḡPēP·PēPeCŕ P'PŷP·, CÍPμCḡPNēPsP·PSPēC... PSPμCÍPīCḡPēCḡC,P»PēPīPēC... CÍPμCḡC†PμPIPs-CÍCŕPrPēPSPSPēC... PīPsPrC-PNē (MACE) C,P° C,,P°PeC,PsCḡPē CḡPēP·PēPeCŕ CḡPsP·PIPēC,PeCŕ P·P»PsCḡPeC-CÍPSPēC... PSPsPIPsCŕC,PIPsCḡPμPSCḡ, P·P° PIPēPSCḡC,PePsPj PIPēPīP°PrPeC-PI, PePsP»Pē PSPμPjP°C" P°P»CHC,PμCḡPSP°C,PēPIPSPēC... PjPμC,PsPrC-PI P»C-PeCŕPīP°PSPSCḡ (PrPēPI. CḡPsP·PrC-P» B«PŷPīPsCÍC-P± P·P°CÍC,PsCÍCŕPīP°PSPSCḡ C,P° PrPsP·PēB»).

PμP°C†C-C"PS C,P°Pj C-P· C,,P°PeC,PsCḡP°PjPē CḡPēP·PēPeCŕ CḡPsP·PIPēC,PeCŕ CÍPμCḡC†PμPIPs-CÍCŕPrPēPSPSPēC... P·P°C...PIPsCḡCḡPīP°PSCḡ P°P±Ps C,,P°PeC,PsCḡP°PjPē CḡPēP·PēPeCŕ CḡPsP·PIPēC,PeCŕ P·P»PsCḡPeC-CÍPSPēC... PSPsPIPsCŕC,PIPsCḡPμPSCḡ (PrPēPI. C,P°PePsP¶ C†PμPNē CḡPsP·PrC-P» B«PŷPμCḡPNēPsP·PSC- PSPμCÍPīCḡPēCḡC,P»PēPIC- CÍPμCḡC†PμPIPs-CÍCŕPrPēPSPSC- PīPsPrC-C— (MACE)B» C,P° B«P—P»PsCḡPeC-CÍPSC- PSPsPIPsCŕC,PIPsCḡPμPSPSCḡB») C,PsC,,P°C†PēC,PēPSC-P± CÍP»C-Pr P·P°CÍC,PsCÍPsPICŕPīP°C,Pē P»PēC€Pμ P·P° PIC-PrCÍCŕC,PSPsCÍC,C- PIC-PrPīPsPIC-PrPSPēC... P°P»CHC,PμCḡPSP°C,PēPIPSPēC... PjPμC,PsPrC-PI P»C-PeCŕPīP°PSPSCḡ.

PμP°C†C-C"PS C,P°Pj P· C,,P°PeC,PsCḡP°PjPē CḡPēP·PēPeCŕ P'PŷP·, PIC-PrPjC-PSPSPēPjPē PIC-Pr MACE P°P±Ps C,,P°PeC,PsCḡC-PI CḡPēP·PēPeCŕ P·P»PsCḡPeC-CÍPSPēC... PSPsPIPsCŕC,PIPsCḡPμPSCḡ, C,PsC,,P°C†PēC,PēPSC-P± CÍP»C-Pr P·P°CÍC,PsCÍPsPICŕPīP°C,Pē P· PsP±PμCḡPμP¶PSC-CÍC,Cḡ. PαP°PeC,PsCḡPē CḡPēP·PēPeCŕ P'PŷP·, PIC-PrPjC-PSPSC- PIC-Pr MACE P°P±Ps C,,P°PeC,PsCḡC-PI CḡPēP·PēPeCŕ P·P»PsCḡPeC-CÍPSPēC... PSPsPIPsCŕC,PIPsCḡPμPSCḡ, PsC...PsPīP»CḡCḡC,CH PīPsPīPμCḡPμPrPSC- PīPsPrC-C— P'PŷP·; PrPs PīCḡCŕPī CḡPēP·PēPeCŕ PSP°P»PμP¶P°C,CH PīP°C†C-C"PS C,Pē, CḡPeC- PīPμCḡPμPSPμCÍP»Pē CÍPμCḡPNēPsP·PSCŕ PsPīPμCḡP°C†C-Cḡ, C-PjPjPsP±C-P»C-P·P°C†C-Cḡ; PīP°C†C-C"PS C,Pē, CḡPeC- P·P°CÍC,PsCÍPsPICŕCḡC,CH PePsPjP±C-PSPsPīP°PSC- PīPsCḡPjPsPSP°P»CHPSCŕ PePsPSC,CḡP°C†PμPīC,PēPIPē P°P±Ps P·P°PjC-CÍPSCŕ PīPsCḡPjPsPSP°P»CHPSCŕ C,PμCḡP°PīC-Cḡ; PīP°C†C-C"PS C,Pē P·C- CÍPīP°PrPePsPīPēPjPē PīPsCḡCŕC€PμPSPSCḡPjPē P·PīPsCḡC,P°PSPSCḡ PeCḡPsPIC-. PμC-Pr C#P°CÍ C,PμCḡP°PīC-C— C,PsC,,P°C†PēC,PēPSC-P±PsPj CÍP»C-Pr PīPμCḡC-PsPrPēC#PSPs PIPēPePsPSCŕPīP°C,Pē PīPsPIC,PsCḡPSPμ PsP±CÍC,PμP¶PμPSPSCḡ PīP°C†C-C"PS C,PI PrP»Cḡ PsC†C-PSPePē CḡPēP·PēPeCŕ P'PŷP·.

PμP°C†C-C"PS C,P°Pj C-P· P Ph C,P° P· PIC-PrPsPjPēPjPē C,,P°PeC,PsCḡP°PjPē CḡPēP·PēPeCŕ P'PŷP· CÍP»C-Pr PIPēPePsPSP°C,Pē P°PSP°P»C-P· PrP»Cḡ PIPēP·PSP°C#PμPSPSCḡ CḡC-PIPSCḡ D-PrPēPjPμCḡP° PīCḡPēP±P»PēP·PSPs C#PμCḡPμP· 12 PjC-CÍCḡC†C-PI PīC-CÍP»Cḡ PīPsC#P°C,PeCŕ C,PμCḡP°PīC-C—. PīPeC%Ps CḡPμP·CŕP»CHC,P°C, C,PμCÍC,Cŕ PSP° D- PrPēPjPμCḡ CÍC,P°PSPsPīPēC,CH $\geq 2 \times P'P_{\text{H}}K_{\text{P}}$, C,Ps PīPμCḡC€ PSC-P¶ PīCḡPēPNēPSCḡC,Pē CḡC-C€PμPSPSCḡ PīCḡPs PīCḡPsPrPsPīP¶PμPSPSCḡ C,PμCḡP°PīC-C— C,PsC,,P°C†PēC,PēPSC-P±PsPj, CÍP»C-Pr PīPμCḡPμPePsPSP°C,PēCÍCḡ, C%Ps

PeP»C-PSC-C†PSP° PePsCḡPëCíC,CH C,P°PePsC— C,PμCḡP°PíC-C— PíPμCḡPμPIPëC%CrC”
C—C— CḡPëP·PëPePë.

PμP°C†C-C”PSC,P°Pj P· PsP·PSP°PeP°PjPë PNë CíPëPjPíC,PsPjP°PjPë P’PÿP· CíP»C-Pr
PSPμPíP°PNëPSPs PIPëPePsPSP°C,Pë PsP±CíC,PμP¶PμPSPSCı C,P° PI CḡP°P·C- PíC-PrPsP·CḡPë
PSP° P’PÿP· PíCḡPëPíPëPSPëC,Pë P·P°CíC,PsCíCíPIP°PSPSCı C,PsC,,P°C†PëC,PëPSC-P±Cí
PSPμP·P°P»PμP¶PSPs PIC-Pr PrPsP·Pë C†Pë PíPsPeP°P·P°PSPSCı, P·P° CıPëPëPj PIC-PS
P·P°CíC,PsCíPsPICíPIP°PICíCı.

PÿCḡPsPjP±PsP· PIPμPS CíC-C,PeC-PIPePë

PμPsPIC-PrPsPjP»CıP»PsCíCı PíCḡPs C,CḡPsPjP±PsP· PIPμPS CíC-C,PeC-PIPePë (PÿP’Pÿ) Cí
PíP°C†C-C”PSC,C-PI, CıPëC- PsC,CḡPëPjCíPIP°P»Pë C,PsC,,P°C†PëC,PëPSC-P± (PrPëPI.
CḡPsP·PrC-P» B«PμPsP±C-C†PSC- CḡPμP°PeC†C-C—B»). PμP°C†C-C”PSC,P°Pj CíP»C-Pr
CḡPμPePsPjPμPSPíCíPIP°C,Pë PSPμPíP°PNëPSPs P·PIPμCḡPSCíC,PëCíCı PíPs PjPμPrPëC†PSCí
PrPsPíPsPjPsPíCí PI CḡP°P·C- PIPëPSPëPePSPμPSPSCı CíPëPjPíC,PsPjC-PI, C%Ps
PjPsP¶CíC,CH PIPëP°P·CíPIP°C,Pë PSP° PÿP’Pÿ.

PÿPμCḡPNëPsP·PSC- C-PSC,,PμPeC†C-C—

PμPsPIC-PrPsPjP»CıP»PsCíCı PíCḡPs CíPμCḡPNëPsP·PSC- PNë C-PSPsPrC- P»PμC,P°P»CHPSC-
C-PSC,,PμPeC†C-C—, CíPíCḡPëC†PëPSPμPSC- P±P°PeC,PμCḡC-P°P»CHPSPëPjPë,
PjC-PePsP±P°PeC,PμCḡC-P°P»CHPSPëPjPë, C-PSPIP°P·PëPIPSPëPjPë PíCḡPëP±PePsPIPëPjPë,
PIC-CḡCíCíPSPëPjPë P°P±Ps C-PSC€PëPjPë CíPjPsPIPSPs PíP°C,PsPíPμPSPSPëPjPë
(PsPíPsCḡC,CíPSC-CíC,PëC†PSPëPjPë) PjC-PeCḡPsPsCḡPíP°PSC-P·PjP°PjPë, Cí
PíP°C†C-C”PSC,C-PI, CıPëC- PsC,CḡPëPjCíPIP°P»Pë C,PμCḡP°PíC-Cḡ
C,PsC,,P°C†PëC,PëPSC-P±PsPj (PrPëPI. CḡPsP·PrC-P» B«PμPsP±C-C†PSC- CḡPμP°PeC†C-C—B»).
P PëP·PëPe PsPíPsCḡC,CíPSC-CíC,PëC†PSPëC... C-PSC,,PμPeC†C-PNë PIPëC%PëPNë PI
P°P·C-P°C,CíCHPePsPjCí PíPμPsPíCḡP°C,,C-C†PSPsPjCí CḡPμPíC-PsPSC- (PrPëPI. CḡPsP·PrC-P»
B«PμPsP±C-C†PSC- CḡPμP°PeC†C-C—B»). PμP°C†C-C”PSC,Pë P· CḡPμPIPjP°C,PsC—PrPSPëPj
P°CḡC,CḡPëC,PsPj, CıPëC- PsC,CḡPëPjCíCḡC,CH PePsCḡC,PëPePsCíC,PμCḡPsC—PrPë,
PjPsP¶CíC,CH P±CíC,Pë CíC...PëP»CHPSPëPjPë PrPs PIPëPSPëPePSPμPSPSCı
C-PSC,,PμPeC†C-PNë.

PkPμ CíP»C-Pr CḡPsP·PíPsC†PëPSP°C,Pë C,PμCḡP°PíC-Cḡ C,PsC,,P°C†PëC,PëPSC-P±PsPj
PíP°C†C-C”PSC,P°Pj P· P°PeC,PëPIPSPëPjPë C-PSC,,PμPeC†C-CıPjPë, P·PsPeCḡPμPjP°
P»PsPeP°P»C-P·PsPIP°PSPëPjPë.

PμPμCḡPμPr PíPsC†P°C,PePsPj C,PμCḡP°PíC-C— CíP»C-Pr CḡPμC,PμP»CHPSPs P·PIP°P¶PëC,Pë
CḡPëP·PëPePë PNë PePsCḡPëCíC,CH PIC-Pr P·P°CíC,PsCíCíPIP°PSPSCı
P»C-PeP°CḡCíCHPePsPíPs P·P°CíPsP±Cí PíP°C†C-C”PSC,P°Pj:

B· P· CḡPμC†PëPrPëPICíCḡC†PëPjPë C-PSC,,PμPeC†C-CıPjPë;

B· P· PSP°CıPIPSC-CíC,CH PI P°PSP°PjPSPμP·C- CíPμCḡPNëPsP·PSPëC... P°P±Ps
PsPíPsCḡC,CíPSC-CíC,PëC†PSPëC... C-PSC,,PμPeC†C-PNë;

B· CıPëC- PíCḡPsP¶PëPIP°P»Pë PI CḡP°PNëPsPSP°C... PμPSPíPμPjC-C†PSPëC...
PjC-PePsP·C-PI P°P±Ps PíPsPrPsCḡPsP¶CíPIP°P»Pë PrPs PSPëC...;

B· CıPëC- PjP°CḡC,CH CíCíPíCíC,PSC- P·P°C...PIPSCḡCḡPIP°PSPSCı, C%Ps
PjPsP¶CíC,CH CḡPsP±PëC,Pë PíP°C†C-C”PSC,C-PI P±C-P»CHC€ CíC...PëP»CHPSPëPjPë

PrPs CḡPsP·PIPëC,PeCř C-PSC,,PμPeC†C-PN̄.

PμC-Pr C‡P°Cḡ C,P° PīC-CḡP»Cḡ C,PμCḡP°PīC-C— C,PsC,,P°C†PëC,PëPSC-P±PsPj CḡP»C-Pr CḡPμC,PμP»CH̄PSPs CḡPīPsCḡC,PμCḡC-PiP°C,Pë P·P° PīP°C†C-C''PSC,P°PjPë PrP»Cḡ CḡP°PSPSCH̄PsPiPs PIPëCḡPIP»PμPSPSCḡ PsP·PSP°Pe C- CḡPëPjPīC,PsPjC-PI C-PSC,,PμPeC†C-C—. PīPeC%Ps PI PīP°C†C-C''PSC,P° CḡPsP·PIPëPIP°C''C,CH̄CḡCḡ CḡPμCḡPN̄PsP·PSP° C-PSC,,PμPeC†C-Cḡ, PsPīPsCḡC,CřPSC-CḡC,PëC‡PSP° C-PSC,,PμPeC†C-Cḡ P°P±Ps CḡPμPīCḡPëCḡ, C,PμCḡP°PīC-Cḡ C†PëPj PīCḡPμPīP°CḡP°C,PsPj CḡP»C-Pr C,PëPjC‡P°CḡPsPiPs PīCḡPëP·CřPīPëPSPëC,Pë. PμP°C†C-C''PSC,Cř, PI CḡPePsPiPs PīC-Pr C‡P°Cḡ C,PμCḡP°PīC-C— C,PsC,,P°C†PëC,PëPSC-P±PsPj CḡPsP·PIPëPIP°C''C,CH̄CḡCḡ PSPsPIP° C-PSC,,PμPeC†C-Cḡ, PīPsC,CḡC-P±PSPs PSPμPīP°PN̄PSPs PIPëPePsPSP°C,Pë PīPsPiPSPμ PrC-P°PiPSPsCḡC,PëC‡PSPμ PsP±CḡC,PμPḡPμPSPSCḡ, CḡPePμ PīC-PrC...PsPrPëC,CH̄ PrP»Cḡ PīP°C†C-C''PSC,C-PI P· PsCḡP»P°P±P»PμPSPëPj C-PjCřPSC-C,PμC,PsPj, CḡPsP·PīPsC‡P°C,Pë PIC-PrPīPsPIC-PrPSCř P°PSC,PëPjC-PëCḡPsP±PSCř C,PμCḡP°PīC-Cḡ C,P° CḡPμC,PμP»CH̄PSPs CḡPīPsCḡC,PμCḡC-PiP°C,Pë P·P° CḡC,P°PSPsPj C,P°PePsPiPs PīP°C†C-C''PSC,P°.

PhCḡPeC-P»CH̄PePë PI P»CḡPrPμPN̄ PīPsC...PëP»PsPiPs PIC-PeCř C,P° PI PīPsPīCḡP»CḡC†C-C— C...PIPsCḡPëC... PSP° C†CřPeCḡPsPIPëPN̄ PrC-P°P±PμC, P·P°PiP°P»PsPj C‡P°CḡC,PsC,P° PIPëPīP°PrPeC-PI PIPëPSPëPePSPμPSPSCḡ C-PSC,,PμPeC†C-PN̄ PīC-PrPIPëC%CřC''C,CH̄CḡCḡ, CḡP»C-Pr P· PsP±PμCḡPμPḡPSC-CḡC,Cḡ P·P°CḡC,PsCḡPsPICřPIP°C,Pë PīCḡPμPīP°CḡP°C, PīC-Pr C‡P°Cḡ P»C-PeCřPIP°PSPSCḡ P»CḡPrPμPN̄ PīPsC...PëP»PsPiPs PIC-PeCř PN̄ PīP°C†C-C''PSC,C-PI P· PrC-P°P±PμC,PsPj (PrPëPI. CḡPsP·PrC-P» B«PμPsP±C-C‡PSC-CḡPμP°PeC†C-C—B»). Ph̄PsPḡP»PëPIC-CḡC,CH̄ P·P°CḡC,PsCḡCřPIP°PSPSCḡ C,PsC,,P°C†PëC,PëPSC-P±Cř PīP°C†C-C''PSC,P°Pj PIC-PePsPj 65 CḡPsPeC-PI C- CḡC,P°CḡCḡPμ CḡP»C-Pr CḡPsP·PiP»CḡPrP°C,Pë P»PëCḡPμ PI CḡP°P·C- PIC-PrCḡCřC,PSPsCḡC,C- PSP°P»PμPḡPSPëC... P°P»CH̄C,PμCḡPSP°C,PëPIPSPëC... PjPμC,PsPrC-PI C,PμCḡP°PīC-C—.

P PëP·PëPe C-PSC,,C-PeCřPIP°PSPSCḡ PjPsPḡPμ PīC-PrPIPëC%CřPIP°C,PëCḡCḡ P·C- P·P±C-P»CH̄CḡPμPSPSCḡPj CḡC,CřPīPμPSCḡ P»C-PjC,,PsPīPμPSC-C—, C,PsPjCř PīC-Pr C‡P°Cḡ PsC†C-PSCḡPIP°PSPSCḡ C-PSPPrPëPIC-PrCřP°P»CH̄PSPsPiPs CḡPëP·PëPeCř PIPëPSPëPePSPμPSPSCḡ C-PSC,,PμPeC†C-C— PI PīP°C†C-C''PSC,P° CḡP»C-Pr CřCḡP°C...PsPICřPIP°C,Pë PrP°PSC- C%PsPrPs PeC-P»CH̄PePsCḡC,C- P»C-PjC,,PsC†PëC,C-PI. PḡCḡPëC,PμCḡC-C— PīCḡPëPīPëPSPμPSPSCḡ C,PμCḡP°PīC-C— C,P° PIPëPePsPSP°PSPSCḡ PjPsPSC-C,PsCḡPëPSPiCř PīCḡPë P»C-PjC,,PsPīPμPSC-C— PSP°PIPμPrPμPSC- PI CḡPsP·PrC-P»C- B«PḡPīPsCḡC-P± P·P°CḡC,PsCḡCřPIP°PSPSCḡ C,P° PrPsP·PëB».

PḡCřP±PμCḡPeCřP»CH̄PsP·

PμPμCḡPμPr PīPsC‡P°C,PePsPj C,PμCḡP°PīC-C— CḡP»C-Pr CḡPμC,PμP»CH̄PSPs P·PIP°PḡPëC,Pë CḡPëP·PëPePë PN̄ PePsCḡPëCḡC,CH̄ PIC-Pr P·P°CḡC,PsCḡCřPIP°PSPSCḡ PīCḡPμPīP°CḡP°C,Cř PīP°C†C-C''PSC,P°Pj:

B· CḡPeC- P±CřP»Pë PI PePsPSC,P°PeC,C- C-P· C...PIPsCḡPëPj PSP° C,CřP±PμCḡPeCřP»CH̄PsP·;

B· CḡPeC- PīCḡPsPḡPëPIP°P»Pë PI CḡP°PN̄PsPSP°C... PμPSPPrPμPjC-C‡PSPsPiPs C,CřP±PμCḡPeCřP»CH̄PsP·Cř P°P±Ps PīPsPrPsCḡPsPḡCřPIP°P»Pë PrPs PSPëC....

PμPμCḡPμPr PīPsC‡P°C,PePsPj P·P°CḡC,PsCḡCřPIP°PSPSCḡ C,PsC,,P°C†PëC,PëPSC-P±Cř C,P° PīC-Pr C‡P°Cḡ PN̄PsPiPs P·P°CḡC,PsCḡCřPIP°PSPSCḡ (P· C-PSC,PμCḡPIP°P»P°PjPë, P·P°P·PSP°C‡PμPSPëPjPë Cř PIC-PrPīPsPIC-PrPSPëC... CḡPμPePsPjPμPSPPrP°C†C-CḡC...) PīP°C†C-C''PSC,P°Pj CḡP»C-Pr PIPëPePsPSCřPIP°C,Pë PsP±CḡC,PμPḡPμPSPSCḡ C-

P°PSP°P»C-P·Pë PrP»C| PIPëC|PIP»PµPSPSC| P»P°C,PµPSC,PSPsC— P°P±Ps
P°PeC,PëPIPSPsC— C-PSC,,PµPeC†C-C—.

PµP°C†C-C°PSC,Pë P· P»P°C,PµPSC,PSPëPj C,C†P±PµC†PeC†P»CHbPsP·PsPj, C† C|PePëC...
P±C†PI PsC,C†PëPjP°PSPëPNë PîPsP·PëC,PëPIPSPëPNë C†PµP·C†P»CHbC,P°C, P°PSP°P»C-P·C†,
PîPµC†PµPr PîPsC†P°C,PePsPj P·P°C†C,PsC†C†PIP°PSPSC| C,PsC,,P°C†PëC,PëPSC-P±C†
PjP°C†C,CHb PîC†PsPNëC,Pë PeC†C†C† C†C,P°PSP°P°C†C,PSPsC—
P°PSC,PëPjC-PePsP±P°PeC,PµC†C-P°P»CHbPSPsC— C,PµC†P°PîC-C—.

P°PsC†C-P»CHbPSC-C†C,CHb PîC†PsC,PëC,C†P±PµC†PeC†P»CHbPsP·PSPsC— C,PµC†P°PîC-C—
PîPµC†PµPr P·P°C†C,PsC†C†PIP°PSPSC|Pj C,PsC,,P°C†PëC,PëPSC-P±C† C,P°PePsP¶ C†P»C-Pr
C†PsP·PîP»C|PSC†C,Pë PrP»C| PîP°C†C-C°PSC,C-PI C-P· PSPµPîP°C,PëPIPSPëPj
C†PµP·C†P»CHbC,P°C,PsPj C,PµC†C,C† PSP° C,C†P±PµC†PeC†P»CHbPsP·, P°P»Pµ PI C|PePëC... PI
P°PSP°PjPSPµP·C- P±C†PI P»P°C,PµPSC,PSPëPNë P°P±Ps P°PeC,PëPIPSPëPNë
C,C†P±PµC†PeC†P»CHbPsP· C- PSPµPjP°C° PîC-PrC,PIPµC†PrP¶PµPSPSC| C,PsPiPs, C%Ps
PîP°C†C-C°PSC, PîC†PsPNëC¶PsPi PSP°P»PµP¶PSPëPNë PeC†C†C† P»C-PeC†PIP°PSPSC|, P°P±Ps
PrP»C| PîP°C†C-C°PSC,C-PI, C† C|PePëC... C†PµP·C†P»CHbC,P°C, C,PµC†C,C†
PSPµPîP°C,PëPIPSPëPNë, P°P»Pµ PîC†PëC†C†C,PSC- C,,P°PeC,PsC†Pë C†PëP·PëPeC†
C-PSC,,C-PeC†PIP°PSPSC| C,C†P±PµC†PeC†P»CHbPsP·PsPj. P PµPePsPjPµPSP°C†C,CHbC†C|
PîC†PsPePsPSC†C†P»CHbC,C†PIP°C,PëC†C| P· PjPµPrPëC†PSPëPj PîC†P°C†C-PIPSPëPePsPj,
C|PePëPNë PjP°C° PrPsC†PIC-Pr P»C-PeC†PIP°PSPSC| C,C†P±PµC†PeC†P»CHbPsP·C†, C%PsP±
PrPsPîPsPjPsPiC,Pë PîC†PëPNëPSC|C,Pë C†C-C¶PµPSPSC| PîC†Ps PrPsC†C-P»CHbPSC-C†C,CHb
PîPsC†P°C,PeC† PîC†PsC,PëC,C†P±PµC†PeC†P»CHbPsP·PSPsC— C,PµC†P°PîC-C— PrP»C|
PePsP¶PSPsPiPs PePsPSPeC†PµC,PSPsPiPs PîP°C†C-C°PSC,P°. PµPsC,C†C-P±PSPs
C†PµC,PµP»CHbPSPs PIC-PrC†C,PµP¶C†PIP°C,Pë PsP·PSP°PePë PNë C†PëPjPiC,PsPjPë
C†PsP·PIPëC,PeC† C,C†P±PµC†PeC†P»CHbPsP·C†, P·PsPeC†PµPjP° PI PîP°C†C-C°PSC,C-PI, C†
C|PePëC... PrPs PîPsC†P°C,PeC† C,PµC†P°PîC-C— P±C†PI PsC,C†PëPjP°PSPëPNë
PSPµPîP°C,PëPIPSPëPNë C†PµP·C†P»CHbC,P°C, C,PµC†C,C† PSP° P»P°C,PµPSC,PSC†
C,C†P±PµC†PeC†P»CHbPsP·PSC† C-PSC,,PµPeC†C-C†.

P PµP°PeC,PëPIP°C†C-C| PIC-C†C†C†PSPsC— C-PSC,,PµPeC†C-C—

Pj PîP°C†C-C°PSC,C-PI, C|PeC- PsC,C†PëPjC†PIP°P»Pë C,PsC,,P°C†PëC,PëPSC-P±
C†PiPsC†C,PµC†C-PîP°P»PëC†C| PIPëPîP°PrPePë C†PµP°PeC,PëPIP°C†C-C—
PIC-C†C†C†PSPëC... C-PSC,,PµPeC†C-PNë C- PIPëPîP°PrPePë C†PµP°PeC,PëPIP°C†C-C—
PIC-C†C†C†C† PîPµC†PîPµC†C† (PSP°PîC†PëPeP»P°Pr, PsPiPµC†C-P·C†C†C†PsPiPs
PiPµC†PîPµC†C†) (PrPëPI. C†PsP·PrC-P» B«PµPsP±C-C†PSC- C†PµP°PeC†C-C—B»).

PŸPµC†PµPr PîP°C†C-C°PSC,C-PI, C|PeC- PsC,C†PëPjC†PIP°P»Pë C,PµC†P°PîC-C†
C,PsC,,P°C†PëC,PëPSC-P±PsPj, P·P°C...PIPSC†C†PIP°PSC-C†C,CHb PSP°
PsPiPµC†C-P·C†C†C†PëPNë PiPµC†PîPµC† PîC-PrPIPëC%C†C°C,CHbC†C| PI C,P°PePëC...
PîC-PrPiC†PîP°C....

B· PîP°C†C-C°PSC,Pë P· PîPîPsPSC-C— P°P±Ps PµPsC†PµC—;

B· PîP°C†C-C°PSC,Pë P· P°P±C†PsP»C†C,PSPsC† PeC-P»CHbPeC-C†C,C†
P»PµPNëPePsC†PëC,C-PI PjPµPSC¶Pµ 1000 PeP»C-C,PëPS/PjPj³ (PrPëPI. C†PsP·PrC-P»
B«PŸPiPsC†C-P± P·P°C†C,PsC†C†PIP°PSPSC| C,P° PrPsP·PëB»);

B· PîP°C†C-C°PSC,Pë C-P· PrPsPIPiPsC,C†PëPIP°P»PëPj C†PµPIPjP°C,PsC—PrPSPëPj
P°C†C,C†PëC,PsPj, C|PeC- C†P°PSC-C¶Pµ PsC,C†PëPjC†PIP°P»Pë PrPIP° P°P±Ps
P±C-P»CHbC¶Pµ P±C-PsP»PsPiC-C†PSPëC... PîC†PsC,PëC†PµPIPjP°C,PëC†PSPëC...
PîC†PµPîP°C†P°C,Pë, C%Ps PjPsPrPëC,,C-PeC†C†C,CHb PîPµC†PµP±C-Pi

P·P°C...PIPsCḡCḡPIP°PSPSCḡ (DMARD);

B· PİP°C†C-C''PSC,Pë, CḡPeC- PsC,CḡPëPjCrPIP°P»Pë C†PµPNë PİCḡPµPİP°CḡP°C, Cr PrPsP·C- 10 PjPi PrPIP° CḡP°P·Pë PSP° PrPsP±Cḡ.

P'PİP»PëPI C,PsC,,P°C†PëC,PëPSC-P±Cḡ PSP° CḡPµP°PeC,PëPIP°C†C-Cḡ C...CḡPsPSC-C†PSPsPiPs PIC-CḡCḡCḡPSPsPiPs PiPµPİP°C,PëC,Cḡ PSPµPIC-PrPsPjPëPNë. PµP°C†C-C''PSC,Pë P· PİPsP·PëC,PëPIPSPëPj CḡPµP·CḡP»CHC,P°C,PsPj CḡPeCḡPëPSC-PSPİPsPiPs C,PµCḡC,Cḡ PSP° PiPµPİP°C,PëC, B P°P±Ps C PSPµ PrPsPİCḡCḡPeP°P»PëCḡCḡ PrPs CḡC†P°CḡC,C- PI PeP»C-PSC-C†PSPëC... PrPsCḡP»C-PrPḡPµPSPSCḡC.... PµPµCḡPµPr PİPsC†P°C,PePsPj C- PİC-Pr C†P°Cḡ C,PµCḡP°PİC-C— C,PsC,,P°C†PëC,PëPSC-P±PsPj CḡP»C-Pr PİPëPePsPSCḡPIP°C,Pë CḡPeCḡPëPSC-PSPİPsPiPµ PsP±CḡC,PµPḡPµPSPSCḡ PSP° PIC-CḡCḡCḡPSPëPNë PiPµPİP°C,PëC, PIC-PrPİPsPIC-PrPSPs PrPs PeP»C-PSC-C†PSPëC... CḡPµPePsPjPµPSPPrP°C†C-PNë.

CµCḡPNëPsP·PSC- PSPµCḡPİCḡPëCḡCḡ,P»PëPIC- CḡPµCḡC†PµPIPs-CḡCḡPrPëPSPSC- PİPsPrC-C— (PIPeP»CḡC†PSPs P· C-PSC,,P°CḡPeC,PsPj PjC-PsPeP°CḡPrP°)

Pj PİP°C†C-C''PSC,C-PI, CḡPeC- PsC,CḡPëPjCrPIP°P»Pë C,PsC,,P°C†PëC,PëPSC-P±, CḡPİPsCḡC,PµCḡC-PİP°P»PëCḡCḡ CḡPµCḡPNëPsP·PSC- PSPµCḡPİCḡPëCḡCḡ,P»PëPIC- CḡPµCḡC†PµPIPs-CḡCḡPrPëPSPSC- PİPsPrC-C— (major adverse cardiovascular events, MACE).

Pj CḡP°PSPPrPsPjC-P·PsPIP°PSPsPjCr PİC-CḡP»CḡCḡPµC''CḡC,CḡP°C†C-PNëPSPsPjCr PrPsCḡP»C-PrPḡPµPSPSC- P±PµP·PİPµPePë P·P° CḡC†P°CḡC,Cḡ PİP°C†C-C''PSC,C-PI C-P· CḡPµPIPjP°C,PsC—PrPSPëPj P°CḡC,CḡPëC,PsPj PIC-PePsPj PIC-Pr 50 CḡPsPeC-PI C- PİCḡPëPSP°PNëPjPSC- PsPrPSPëPj PrPsPrP°C,PePsPiPëPj C,,P°PeC,PsCḡPsPj CḡPëP·PëPeCḡ CḡPµCḡC†PµPIPs-CḡCḡPrPëPSPSPëC... CḡCḡPeP»P°PrPSPµPSCH CḡPİPsCḡC,PµCḡC-PİP°P»PsCḡCḡ PİC-PrPIPëC%PµPSPSCḡ C†P°CḡC,PsC,Pë PİPëPSPëPePSPµPSPSCḡ C-PSC,,P°CḡPeC,Cḡ PjC-PsPeP°CḡPrP° PİC-Pr C†P°Cḡ P·P°CḡC,PsCḡCḡPIP°PSPSCḡ C,PsC,,P°C†PëC,PëPSC-P±Cḡ PİPsCḡC-PIPSḡPSPs P· C-PSPİC-P±C-C,PsCḡP°PjPë PαPḡPµ (PrPëPI. CḡPsP·PrC-P» B«PµPsP±C-C†PSC- CḡPµP°PeC†C-C—B»). PµP°C†C-C''PSC,P°Pj PIC-PePsPj 65 CḡPsPeC-PI C- CḡC,P°CḡCḡPµ, PİP°C†C-C''PSC,P°Pj, CḡPeC- PeCḡCḡCḡCḡ,CH P°P±Ps PeCḡCḡPëP»Pë PİCḡPsC,CḡPİPsPj C,CḡPëPIP°P»PsPiPs C†P°CḡCḡ PI PjPëPSCḡP»PsPjCr, P° C,P°PePsPḡ PİP°C†C-C''PSC,P°Pj P· P°C,PµCḡPsCḡPeP»PµCḡPsC,PëC†PSPëPjPë CḡPµCḡC†PµPIPs-CḡCḡPrPëPSPSPëPjPë P·P°C...PIPsCḡCḡPIP°PSPSCḡPjPë PI P°PSP°PjPSPµP·C- P°P±Ps C-PSCḡPëPjPë C,,P°PeC,PsCḡP°PjPë CḡPëP·PëPeCḡ CḡPµCḡC†PµPIPs-CḡCḡPrPëPSPSPëC... CḡCḡPeP»P°PrPSPµPSCH C,PsC,,P°C†PëC,PëPSC-P± CḡP»C-Pr P·P°CḡC,PsCḡPsPICḡPIP°C,Pë P»PëCḡPµ P·P° PIC-PrCḡCḡC,PSPsCḡC,C- PIC-PrPİPsPIC-PrPSPëC... P°P»CHC,PµCḡPSP°C,PëPIPSPëC... PjPµC,PsPrC-PI P»C-PeCḡPIP°PSPSCḡ.

P—P»PsCḡPeC-CḡPSC- PSPsPiPsCḡC,PIPsCḡPµPSPSCḡ C,P° P»C-PjC,,PsPİCḡPsP»C-C,,PµCḡP°C,PëPIPSC- P·P°C...PIPsCḡCḡPIP°PSPSCḡ

PḡPsC,,P°C†PëC,PëPSC-P± PjPsPḡPµ PİPİP»PëPIP°C,Pë PSP° P·PrP°C,PSC-CḡC,CH PsCḡPİP°PSC-P·PjCr PİPµCḡPµCḡPePsPrPḡP°C,Pë CḡPsP·PIPëC,PeCḡ P·P»PsCḡPeC-CḡPSPëC... PSPsPiPsCḡC,PIPsCḡPµPSCH.

Pj CḡP°PSPPrPsPjC-P·PsPIP°PSPsPjCr PİC-CḡP»CḡCḡPµC''CḡC,CḡP°C†C-PNëPSPsPjCr PrPsCḡP»C-PrPḡPµPSPSC- P±PµP·PİPµPePë P·P° CḡC†P°CḡC,Cḡ PİP°C†C-C''PSC,C-PI C-P· CḡPµPIPjP°C,PsC—PrPSPëPj P°CḡC,CḡPëC,PsPj PIC-PePsPj PIC-Pr 50 CḡPsPeC-PI C- PİCḡPëPSP°PNëPjPSC- PsPrPSPëPj PrPsPrP°C,PePsPiPëPj C,,P°PeC,PsCḡPsPj CḡPëP·PëPeCḡ

PyP°PePsP¶ C¶PµPePsPjPµPSPPrCfC”C,CHCfC¶P· PsP±PµC¶PµP¶PSC-CfC,C¶P·P°CfC,PsCfPsPICrfPIP°C,Pë C†PµPNë P»C-PeP°C¶CfCHPePePNë P·P°CfC-P±PiP°C†C-C”PSC,P°Pj P· C...C¶PµPSC-C†PSPëPjPë P·P°C...PIPsC¶C¶PIP°PSPSC¶PjPë P»PµPiPµPSC¶ PI P°PSP°PjPSPµP·C-, PsCfPeC-P»CHPePë PIPsPSPë PjPsP¶CfC,CH P±CfC,Pë P±C-P»CHC€ CfC...PëP»CHPSPëPjPë PrPs C¶PµP·PIPëC,PeCf C-PSC,,PµPeC†C-PNë. PµPsPIC-PrPsPjP»C¶P»PsCfC¶ PiC¶Pµ PIPëPiP°PrPePë C-PSC,PµC¶CfC,PëC†C-P°P»CHPSPSc—C...PIPsC¶PµP±Pë P»PµPiPµPSC¶ (PrPµC¶PeC- P· PSPëC... PjP°P»Pë P»PµC,P°P»CHPSC-PSP°CfP»C-PrPePë) Cf PiP°C†C-C”PSC,C-PI, C¶PeC- PsC,C¶PëPjCfPIP°P»Pë C,PsC,,P°C†PëC,PëPSC-P± Cf PeP»C-PSC-C†PSPëC... PrPsCfP»C-PrP¶PµPSPSC¶C... C%oPsPrPs PiPsPeP°P·P°PSPSC¶ P Ph C- PI PiC-CfP»C¶C¶PµC”CfC,C¶P°C†C-PNëPSPëPNë PiPµC¶C-PsPr, C...PsC†P° C¶PµP»CH C-PSPiC-P±CfPIP°PSPSC¶ C¶PSCfCf-PeC-PSP°P· (JAK) Cf C†PëC... PIPëPiP°PrPeP°C... PSPµPIC-PrPsPjP°. P’C-PrPsPjPs, C%oPs PiP°C†C-C”PSC,Pë P°P·C-PNëCfCHPePsPiPs PiPsC...PsPrP¶PµPSPSC¶ P· P Ph PjP°CHC,CH PIPëC%oPëPNë C¶PëP·PëPe C¶PµP·PIPëC,PeCf C-PSC,PµC¶CfC,PëC†C-P°P»CHPSPSc— C...PIPsC¶PµP±Pë P»PµPiPµPSC¶, C,PsPjCf P·P°CfC,PsCfPsPICrfPIP°C,Pë C†PµPNë PiC¶PµPiP°C¶P°C, C,P°PePëPj

ΠῖΠ°C†C-C''PSC,P°Pj CΓP»C-Pr P· PsP±PμCῡPμP¶PSC-CΓC,CḤ.

PμPμCῡC,,PsCῡP°C†C-CΠ CΓC,C-PSPsPe C€P»CΓPSPePsPIPs-PeP€C€PePsPIPsPiPs C,CῡP°PeC,Cr

Pj PeP»C-PSC-C‡PSP€C... PrPsCΓP»C-PrP¶PμPSPSCΠC... ΠῖPsPIC-PrPsPjP»CΠP»PsCΓCΠ ΠῖCῡPs
PIP€ΠῖP°PrPeP€ ΠῖPμCῡC,,PsCῡP°C†C-C— CΓC,C-PSPsPe C€P»CΓPSPePsPIPs-PeP€C€PePsPIPsPiPs
C,CῡP°PeC,Cr, C...PsC‡P° CῡPsP»CḤ C-PSPIC-P±CΓPIP°PSPSCΠ JAK Cr C†P€C...
PIP€ΠῖP°PrPeP°C... PSPμPIC-PrPsPjP°. PŷPsC,,P°C†P€C,P€PSC-P± CΓP»C-Pr
P·P°CΓC,PsCΓPsPICrPIP°C,P€ P· PsP±PμCῡPμP¶PSC-CΓC,CḤ ΠῖP°C†C-C''PSC,P°Pj, Cr CΠPeP€C...
PjPsP¶Pμ P±CΓC,P€ ΠῖC-PrPIP€C%PμPSP€PN€ CῡP€P·P€Pe ΠῖPμCῡC,,PsCῡP°C†C-C—
CΓC,C-PSPsPe C€P»CΓPSPePsPIPs-PeP€C€PePsPIPsPiPs C,CῡP°PeC,Cr (PSP°ΠῖCῡP€PeP»P°Pr,
ΠῖP°C†C-C''PSC,P°Pj C-P· PrP€PIPμCῡC,P€PeCΓP»C-C,PsPj ΠῖP°PSP°PjPSPμP·C-;
ΠῖP°C†C-C''PSC,P°Pj, CΠPeC- PsPrPSPsC‡P°CΓPSPs PsC,CῡP€PjCΓCḤ,CḤ
PePsCῡC,P€PePsCΓC,PμCῡPsC—PrP€ C,P°/P°P±Ps PSPμCΓC,PμCῡPsC—PrPSC-
ΠῖCῡPsC,P€P·P°ΠῖP°P»CḤPSC- ΠῖCῡPμΠῖP°CῡP°C,P€). PμP°C†C-C''PSC,P°Pj, Cr CΠPeP€C...
P·BḤ™ CΠPIP€P»P€CΓCΠ PSPsPIC- PsP·PSP°PeP€ PN€ CΓP€PjΠῖC,PsPjP€ P· P±PsPeCΓ
C€P»CΓPSPePsPIPs-PeP€C€PePsPIPsPiPs C,CῡP°PeC,Cr, CΓP»C-Pr PSPμΠῖP°PN€PSPs
PIP€PePsPSP°C,P€ PsP±CΓC,PμP¶PμPSPSCΠ PrP»CΠ CῡP°PSPSCḤPsPiPs PIP€CΠPIP»PμPSPSCΠ
ΠῖPμCῡC,,PsCῡP°C†C-C— CΓC,C-PSPsPe C€P»CΓPSPePsPIPs-PeP€C€PePsPIPsPiPs C,CῡP°PeC,Cr.

PμPμCῡPμP»PsPjP€

Pj ΠῖP°C†C-C''PSC,C-Πῖ, CΠPeC- PsC,CῡP€PjCΓPIP°P»P€ C,PsC,,P°C†P€C,P€PSC-P±,
CΓΠῖPsCΓC,PμCῡC-ΠῖP°P»P€CΓCΠ ΠῖPμCῡPμP»PsPjP€. PŷPsC,,P°C†P€C,P€PSC-P± CΓP»C-Pr P·
PsP±PμCῡPμP¶PSC-CΓC,CḤ P·P°CΓC,PsCΓPsPICrPIP°C,P€ ΠῖP°C†C-C''PSC,P°Pj P·
PIC-PrPsPjP€PjP€ C,,P°PeC,PsCῡP°PjP€ CῡP€P·P€PeCΓ ΠῖPμCῡPμP»PsPjC-Πῖ, CΠPe-PsC,
PsCΓPsP±P°Pj P»C-C,PSCHPsPiPs PIC-PeCΓ, P¶C-PSPeP°Pj C- ΠῖP°C†C-C''PSC,P°Pj, CΠPeC-
P·P°CΓC,PsCΓPsPICrCḤ,CḤ PePsCῡC,P€PePsCΓC,PμCῡPsC—PrP€, PSPμP·P°P»PμP¶PSPs PIC-Pr
ΠῖPsPeP°P·P°PSPSCΠ PrPs P·P°CΓC,PsCΓCΓPIP°PSPSCΠ C,P° PrPsP·P€ ΠῖCῡPμΠῖP°CῡP°C,Cr.

PμPμC‡C-PSPePsPIC- C,,PμCῡPjPμPSC,P€

PŷPμCῡP°ΠῖC-CΠ C,PsC,,P°C†P€C,P€PSC-P±PsPj P±CΓP»P° P°CΓPsC†C-PN€PsPIP°PSP° P·C-
P·P±C-P»CḤC€PμPSPSCΠPj C‡P°CΓC,PsC,P€ PIP€ΠῖP°PrPeC-Πῖ ΠῖC-PrPIP€C%PμPSPSCΠ
CῡC-PIPSCΠ ΠῖPμC‡C-PSPePsPIP€C... C,,PμCῡPjPμPSC,C-Πῖ Cr PrPμCΠPeP€C...
ΠῖP°C†C-C''PSC,C-Πῖ (PrP€Πῖ. CῡPsP·PrC-P» B«PμPsP±C-C‡PSC- CῡPμP°PeC†C-C—B»). PŷP»C-Pr
P· PsP±PμCῡPμP¶PSC-CΓC,CḤ CῡPsP·ΠῖP»CΠPrP°C,P€ ΠῖP€C,P°PSPSCΠ ΠῖCῡPs ΠῖPsC‡P°C,PsPe
C,PμCῡP°ΠῖC-C— C,PsC,,P°C†P€C,P€PSC-P±PsPj Cr ΠῖP°C†C-C''PSC,C-Πῖ C-P·
ΠῖC-PrPIP€C%PμPSP€PjP€ CῡC-PIPSCΠPjP€
P°P»P°PSC-PSP°PjC-PSPsC,CῡP°PSCΓC,,PμCῡP°P·P€ (PḥP·Pŷ) P°P±Ps
P°CΓΠῖP°CῡC,P°C,P°PjC-PSPsC,CῡP°PSCΓC,,PμCῡP°P·P€ (PḥPŷPŷ), PsCΓPsP±P»P€PIPs PSP°
C,P»C- PsPrPSPsC‡P°CΓPSPsPiPs P·P°CΓC,PsCΓCΓPIP°PSPSCΠ ΠῖPsC,PμPSC†C-PN€PSPs
ΠῖPμΠῖP°C,PsC,PsPeCΓP€C‡PSP€C... P»C-PeP°CῡCΓCḤPeP€C... P·P°CΓPsP±C-Πῖ, CΠPe-PsC,
PjPμC,PsC,CῡPμPeCΓP°C,. PμC-CΓP»CΠ ΠῖPsC‡P°C,PeCΓ C,PμCῡP°ΠῖC-C—
CῡPμPePsPjPμPSPPrCΓC,CḤCΓCΠ P·PrC-PN€CΓPSCḤPIP°C,P€ CῡCΓC,P€PSPSP€PN€
PjPsPSC-C,PsCῡP€PSPi P±C-PsC...C-PjC-C‡PSP€C... ΠῖPsPeP°P·PSP€PeC-Πῖ C,,CΓPSPeC†C-C—
ΠῖPμC‡C-PSPeP€ C- CΠPePSP°PN€C€PIP€PrC€Pμ P·BḤ™ CΠCΓCΓPIP°C,P€ ΠῖCῡP€C‡P€PSP€
P±CΓPrCḤ-CΠPePsPiPs CΓΠῖPsCΓC,PμCῡPμP¶CΓPIP°PSPsPiPs ΠῖC-PrPIP€C%PμPSPSCΠ
CῡC-PIPSCΠ ΠῖPμC‡C-PSPePsPIP€C... C,,PμCῡPjPμPSC,C-Πῖ PrP»CΠ PIP€CΠPIP»PμPSPSCΠ
PjPsP¶P»P€PIP€C... PIP€ΠῖP°PrPeC-Πῖ PjPμPrP€PeP°PjPμPSC,PsP·PSPsPiPs CrCῡP°P¶PμPSPSCΠ
ΠῖPμC‡C-PSPeP€. ΠῖPeC%Ps C'' ΠῖC-PrPsP·CῡP° PSP° PjPμPrP€PeP°PjPμPSC,PsP·PSPμ
CΓCῡP°P¶PμPSPSCΠ ΠῖPμC‡C-PSPeP€, P·P°CΓC,PsCΓCΓPIP°PSPSCΠ C,PsC,,P°C†P€C,P€PSC-P±CΓ

СГР»С-Пр ПСГПёПіПёПСПёС,Пё, ПрПсPePё С†PµPNё ПрС-Р°PiPSPsP· PSPµ P±C†PrPµ
PIPёPeP»СГС†PµPSPs.

Р°С-РіPµСГС†C†C,Р»PёPIC-СГС,СГ

PJ ПіС-СГР»СГСГPµС"СГС,СГР°С†С-PNёPSPёPNё ПіPµСГС-PsPr ПіPsPIC-ПрPsPjP»СГP»PsСГСГ
ПіСГPs PIPёPiP°PrPePё PIPёPSPёPePSPµPSPSCГ СГPµP°PeC†С-PNё
PiC-РіPµСГС†C†C,Р»PёPIPsСГС,С-, ПіPsPIBГ™ СГP·P°PSC- С-Р· P·P°СГС,PsСГСГPIP°PSPSCГPj
C,PsC,,P°С†PёC,PePSC-P±C†. PhP»PµСГPiC-С†PSC- СГPµP°PeC†С-С— PIPёP»СГС†P°P»Pё
P°PSPiC-PsPSPµPICГPsC,PeC†PSPёPNё PSP°P±СГСГPё С- PeСГPsPіPёPIBГ™ СГPSPeC†;
PIPёPSPёPeP°P»Pё СГPµСГPNёPsP·PSC- СГPµP°PeC†С-С—. PJ СГР°P·С- PIPёPSPёPePSPµPSPSCГ
P±C†PrСГ-СГPёPsC— СГPµСГPNёPsP·PSPsC— P°P»PµСГPiC-С†PSPsC—
P°P±Ps P°PSP°С,С-Р»P°PeC,PeC†PSPsC— СГPµP°PeC†С-С— P·P°СГС,PsСГСГPIP°PSPSCГ
C,PsC,,P°С†PёC,PePSC-P±C† СГР»С-Пр PSPµPiP°PNёPSPs ПіСГПёПіPёPSPёС,Пё.

Р>P°P±PsСГР°С,PsСГPSC- PіP°СГР°PjPµC,СГPё

P>С-PjC,,PsC†PёC,Pe

PŷPµСГР°PіC-СГ C,PsC,,P°С†PёC,PePSC-P±PsPj P±C†P»P° P°СГPsC†С-PNёPsPIP°PSP° P·С-
P·P±С-Р»СГСёPµPSPSCГPj C†P°СГС,PsC,Pe PIPёPSPёPePSPµPSPSCГ P»С-PjC,,PsPіPµPSC-С—
PіPsСГС-PIPSCГPSPs P· PіP»P°С†PµP±Ps. PљС-Р»СГPeC-СГС,СГ P»С-PjC,,PsC†PёC,С-PI
PjPµPSCёPµ 750 PeP»С-С,PePS/PjPj³ P±C†P»P° P°СГPsC†С-PNёPsPIP°PSP°
P· ПіС-ПрPIPёC%PµPSPsСГ C†P°СГС,PsC,PsСГ PIPёPSPёPePSPµPSPSCГ СГPµСГPNёPsP·PSPёC...
С-PSC,,PµPeC†С-PNё. P PµPePsPjPµPSPPrC†С"С,СГСГСГ PSPµ ПіPsC†PePSP°С,Pe C,P° PSPµ
ПіСГPsPrPsPIP¶C†PіP°С,Pe C,PµСГР°PіC-СГ C,PsC,,P°С†PёC,PePSC-P±PsPj ПіP°С†С-С"PSC,P°Pj,
C† СГPёPeC... ПіС-ПрC,PIPµСГPrP¶PµPSP° P°P±СГPsP»СГС,PSР° PeC-Р»СГPeC-СГС,СГ
P»С-PjC,,PsC†PёC,С-PI СГС,P°PSPsPIPёC,СГ PjPµPSCёPµ 750 PeP»С-С,PePS/PjPj³.
PљС-Р»СГPeC-СГС,СГ P»С-PjC,,PsC†PёC,С-PI СГР»С-Пр PePsPSC,СГPsP»СГPіP°С,Pe PSP°
PIPёC...С-ПрPSPsPjC† СГС-PIPSC- С,P° PePsP¶PSC- 3 PjC-СГСГС†С- ПіС-СГР»СГ С†СГPsPіPs.
P PµPePsPjPµPSPPrP°С†С-С— C%PsPrPs PePsСГPёPiC†PіP°PSPSCГ ПрPsP·Pё P·P°P»PµP¶PSPs
PIC-Пр PeC-Р»СГPePsСГС,С- P»С-PjC,,PsC†PёC,С-PI ПрPёPI. C†
СГPsP·ПрС-Р»С- B«PŷPіPsСГС-P± P·P°СГС,PsСГСГPіP°PSPSCГ C,P° ПрPsP·PёB».

PќPµPNёC,СГPsC,,С-Р»Pё

PŷPµСГР°PіC-СГ C,PsC,,P°С†PёC,PePSC-P±PsPj P±C†P»P° P°СГPsC†С-PNёPsPIP°PSP° P·С-
P·P±С-Р»СГСёPµPSPSCГPj C†P°СГС,PsC,Pe PIPёPSPёPePSPµPSPSCГ
PSPµPNёC,СГPsPіPµPSC-С— (PeC-Р»СГPeC-СГС,СГ PSPµPNёC,СГPsC,,С-Р»С-PI PjPµPSCёPµ
2000 PeP»С-С,PePS/PjPj³) ПіPsСГС-PIPSCГPSPs P· PіP»P°С†PµP±Ps. PќPµ
СГPµPePsPjPµPSPPrC†С"С,СГСГСГ СГPsP·ПіPsC†PePSP°С,Pe C,PµСГР°PіC-СГ
C,PsC,,P°С†PёC,PePSC-P±PsPj ПрPsСГPsСГР»PёPj ПіP°С†С-С"PSC,P°Pj С-Р·
P°P±СГPsP»СГС,PSРсГ PeC-Р»СГPeC-СГС,СГ PSPµPNёC,СГPsC,,С-Р»С-PI (PhPљPќ)
PjPµPSCёPµ 1000 PeP»С-С,PePS/PjPj³ C,P° ПіP°С†С-С"PSC,P°Pj ПрPёC,СГС†PsPіPs PIC-PeC† P·
PhPљPќ PjPµPSCёPµ 1200 PeP»С-С,PePS/PjPj³. PhPљPќ СГР»С-Пр PePsPSC,СГPsP»СГPіP°С,Pe
PSP° PIPёC...С-ПрPSPsPjC† СГС-PIPSC-, ПіС-СГР»СГ СГ 4БГ"8 C,PeP¶PSC-PI C,PµСГР°PіC-С— C,P°
PePsP¶PSC- 3 PjC-СГСГС†С- ПіС-СГР»СГ С†СГPsPіPs. P PµPePsPjPµPSPPrP°С†С-С— C%PsPrPs
PePsСГPёPiC†PіP°PSPSCГ ПрPsP·Pё P·P°P»PµP¶PSPs PIC-Пр СГС-PIPSCГ PhPљPќ (ПрPёPI. C†
СГPsP·ПрС-Р»С- B«PŷPіPsСГС-P± P·P°СГС,PsСГСГPіP°PSPSCГ C,P° ПрPsP·PёB»).

P°PµPjPsPіP»PsP±С-PS

PŷPµCĤP°PīC-Cl C,PsC,,P°C†PēC,PēPSC-P±PsPj P±C†P»P° P°C†PsC†C-PNēPsPIP°PSP° P·C-
 P·PSPēP¶PµPSPSClPj CĤC-PIPSCl PiPµPjPsPiP»PsP±C-PSCr. PkPµ
 CĤPµPePsPjPµPSPrC†C”C,ChC†Cl CĤPsP·PiPsC†PēPSP°C,Pē C,PµCĤP°PīC-CĤ
 C,PsC,,P°C†PēC,PēPSC-P±PsPj PrPsCĤPsC†P»PēPj PiP°C†C-C”PSC,P°Pj C-P· CĤC-PIPSPµPj
 PiPµPjPsPiP»PsP±C-PSCr PjPµPSCēPµ 9 Pi/PrP» C- PiP°C†C-C”PSC,P°Pj PrPēC,ClC†PsPiPs
 PIC-PeC† P· CĤC-PIPSPµPj PiPµPjPsPiP»PsP±C-PSCr PjPµPSCēPµ 10 Pi/PrP». P C-PIPµPSCĤ
 PiPµPjPsPiP»PsP±C-PSCr C†P»C-Pr PePsPSC,CĤPsP»CĤPIP°C,Pē PSP° PIPēC...C-PrPSPsPjC†
 CĤC-PIPSC-, PiC-C†P»Cl 4bĤ”8 C,PēP¶PSC-PI C,PµCĤP°PīC-C— C,P° PePsP¶PSC-
 3 PjC-C†ClC†C- PiC-C†P»Cl C†CHPsPiPs. P PµPePsPjPµPSPrP°C†C-C— C%oPsPrPs
 PePsCĤPēPiC†PIP°PSPSCl PrPsP·Pē P·P°P»PµP¶PSPs PIC-Pr CĤC-PIPSCl
 PiPµPjPsPiP»PsP±C-PSCr PrPēPI. C† CĤPsP·PrC-P»C- B«PŷPiPsC†C-P±
 P·P°C†C,PsC†C†PIP°PSPSCl C,P° PrPsP·PēB».

PĥPsPSC-C,PsCĤPēPSPi CĤC-PIPSCl P»C-PiC-PrC-PI

PŷPµCĤP°PīC-Cl C,PsC,,P°C†PēC,PēPSC-P±PsPj P±C†P»P° P°C†PsC†C-PNēPsPIP°PSP° P·C-
 P·P±C-P»CHCēPµPSPSClPj CĤC-PIPSC-PI P»C-PiC-PrC-PI, ClPe-PsC, P·P°PiP°P»CHPSPēPNē
 C...PsP»PµC†C,PµCĤPēPS, C...PsP»PµC†C,PµCĤPēPS P»C-PiPsPiCĤPsC,PµC—PSC-PI
 PSPēP·CHPePsC— C%oC-P»CHPSPsC†C,C- (P>PµPkP©) C- C...PsP»PµC†C,PµCĤPēPS
 P»C-PiPsPiCĤPsC,PµC—PSC-PI PIPēC†PsPePsC— C%oC-P»CHPSPsC†C,C- (P>PµP’P©).
 PĥP°PeC†PēPjP°P»CHPSPēPNē PµC,,PµPeC, P·P°P·PIPēC†P°PNē C†PiPsC†C,PµCĤC-PiP°PIC†Cl
 PiCĤPsC,ClPiPsPj 6 C,PēP¶PSC-PI PiC-C†P»Cl PiPsC†P°C,PeC† C,PµCĤP°PīC-C—. PĥC†C-PSPeC†
 P»C-PiC-PrPSPsPiPs PiCĤPsC,,C-P»CĤ PiPsC,CĤC-P±PSPs PIPēPePsPSC†PIP°C,Pē C†PµCĤPµP·
 8 C,PēP¶PSC-PI PiC-C†P»Cl PiPsC†P°C,PeC† C,PµCĤP°PīC-C— C,PsC,,P°C†PēC,PēPSC-P±PsPj.
 P>C-PeC†PIP°PSPSCl PiC-PiPµCĤP»C-PiC-PrPµPjC-C— C†P»C-Pr PiCĤPsPiPsPrPēC,Pē
 PIC-PrPiPsPIC-PrPSPs PrPs PeP»C-PSC-C†PSPēC... CĤPµPePsPjPµPSPrP°C†C-PNē.
 PµC-PrPIPēC%oPµPSC- CĤC-PIPSC- P·P°PiP°P»CHPSPsPiPs C...PsP»PµC†C,PµCĤPēPSCr C,P°
 C...PsP»PµC†C,PµCĤPēPSCr P>PµPkP©, P°C†PsC†C-PNēPsPIP°PSC-
 P· C,PsC,,P°C†PēC,PēPSC-P±PsPj, PjPsP¶PSP° P·PjPµPSCēPēC,Pē PrPs CĤC-PIPSCl, ClPePēPNē
 P±C†PI PrPs PiPsC†P°C,PeC† C,PµCĤP°PīC-C— PiCĤPµPiP°CĤP°C,PsPj PĥC†PµP»CHClPSP·,
 P·P° PrPsPiPsPjPsPiPsCĤ P·P°C†C,PsC†C†PIP°PSPSCl C†C,P°C,PēPSC-PI.

P”C-PiPsPiP»C-PePµPjC-Cl PI PiP°C†C-C”PSC,C-PI, ClPeC- PsC,CĤPēPjC†CĤC,Ch P»C-PeC†PIP°PSPSCl C†C†PeCĤPsPiPsPiPs PrC-P°P±PµC,C†

PµPsPIC-PrPsPjP»ClP»PsC†Cl PiCĤPs PIPēPiP°PrPePē PiC-PiPsPiP»C-PePµPjC-C— PiC-C†P»Cl
 PiPsC†P°C,PeC† C,PµCĤP°PīC-C— C,PsC,,P°C†PēC,PēPSC-P±PsPj C† PiP°C†C-C”PSC,C-PI, ClPeC-
 PsC,CĤPēPjC†PIP°P»Pē PiCĤPµPiP°CĤP°C,Pē PrP»Cl P»C-PeC†PIP°PSPSCl C†C†PeCĤPsPiPsPiPs
 PrC-P°P±PµC,C†. Pj CĤP°P·C- CĤPsP·PIPēC,PeC† PiC-PiPsPiP»C-PePµPjC-C— PjPsP¶Pµ P±C†C,Pē
 PSPµPsP±C...C-PrPSP° PePsCĤPµPeC†C-Cl PrPsP·Pē PiCĤPsC,PēPrC-P°P±PµC,PēC†PSPsPiPs
 PiCĤPµPiP°CĤP°C,C†.

P’P°PeC†PēPSP°C†C-Cl

PµPµCĤPµPr PiPsC†P°C,PePsPj C,PµCĤP°PīC-C— C,PsC,,P°C†PēC,PēPSC-P±PsPj C†C†C-Pj
 PiP°C†C-C”PSC,P°Pj, PsC†PsP±P»PēPIPs PiP°C†C-C”PSC,P°Pj C-P·
 PiPsP»C-P°CĤC,PēPeC†P»ClCĤPSPsCĤ C,,PsCĤPjPsCĤ CĤPIPµPSC-P»CHPSPsPiPs
 C-PrC-PsPiP°C,PēC†PSPsPiPs P°CĤC,CĤPēC,C†, CĤPµPePsPjPµPSPrC†C”C,ChC†Cl
 PIPēPePsPSP°C,Pē PIC†C- C%oPµPiP»PµPSPSCl PIC-PrPiPsPIC-PrPSPs PrPs C†PēPSPSPēC...
 CĤPµPePsPjPµPSPrP°C†C-PNē C%oPsPrPs C-PjC†PSC-P·P°C†C-C—. P,,
 CĤPµPePsPjPµPSPrP°C†C-C— PSPµ P·P°C†C,PsC†PsPIC†PIP°C,Pē P¶PēPIC- PIP°PeC†PēPSPē
 PsPrPSPsC†P°C†PSPs P· C,PsC,,P°C†PēC,PēPSC-P±PsPj. PµC-Pr C†P°C† PiCĤPēPNēPSClC,C,Cl

P—P° PİPsCİPİP»P°PSPSCİPİ <https://www.pfizer.ua/2216> P·PSP°C...PsPrPİC,CHCİCİ

C-PSC,,PsCḡPjP°C†C-PNḡPSP° PḡP°Pjḡḡ™ CḡC,PeP° PrP»Cḡ PḡP°C†C-C"ḡPSC,P°, CḡPeCḡ
CḡPḡPePsPjPḡPSPPrCḡC",CHCḡCḡ P·P°PḡPsPIPSPḡC,Pḡ C- PḡPsPeP°P·CḡPIP°C,Pḡ
P»C-PeP°CḡCḡ.

***P-P°CḡC,PsCḡCḡPIP°PSPSCḡ Cḡ PḡPḡCḡC-PsPr PIP°PiC-C,PSPsCḡC,C- P°P±Ps
PḡPsPrCḡPIP°PSPSCḡ PiCḡCḡPrPrCḡ.***

P°P°PiC-C,PSC-CḡC,CH

PḡC,P°PSPPrP°CḡC,PSPḡC... C- PSP°P»PḡPḡPSPḡPj CḡPḡPSPsPj
PePsPSC,CḡPsP»CHPsPIP°PSPḡC... PrPsCḡP»C-PrPḡPḡPSCḡ P·P°CḡC,PsCḡCḡPIP°PSPSCḡ
C,PsC,,P°C†PḡC,PḡPSC-P±Cḡ PIP°PiC-C,PSPḡPj PḡC-PSPeP°Pj PSPḡ PḡCḡPsPIPPrPḡP»PsCḡCḡ.
P·CḡP»Ps PḡPsPeP°P·P°PSPs, CḡḡPs C,PsC,,P°C†PḡC,PḡPSC-P± CḡPḡCḡPḡCḡPḡPSCḡC"
C,PḡCḡP°C,PsPiPḡPSPSC- PḡC,,PḡPeC,Pḡ PI CḡḡCḡCḡC-PI C- PeCḡPsP»PḡPeC-PI C-
PIPḡP»PḡPIP°C" PSP° PḡPsP»PsPiPḡ, P° C,P°PePsPḡ PḡPḡCḡPḡ/PḡPsCḡC,PSP°C,P°P»CHPSPḡPNḡ
CḡPsP·PIPḡC,PsPe PḡPsC,PsPjCḡC,PIP°.

PḡPe P·P°PḡPsP±C-PḡPSPḡPNḡ P·P°C...C-Pr P·P°CḡC,PsCḡCḡPIP°PSPSCḡ
C,PsC,,P°C†PḡC,PḡPSC-P±Cḡ PiC-Pr CḡP°Cḡ PIP°PiC-C,PSPsCḡC,C- PḡCḡPsC,PḡPḡPsPeP°P·P°PSPs
(PrPḡPI. CḡPsP·PrC-P» B«PḡCḡPsC,PḡPḡPsPeP°P·P°PSPSCḡB»).

P-C-PSPePḡ CḡPḡPiCḡPsPrCḡPeC,PḡPIPSPsPiPs PIC-PeCḡ / PePsPSC,CḡP°C†PḡPiC†C-Cḡ PrP»Cḡ
PḡC-PSPsPe

P-C-PSPeP°Pj CḡPḡPiCḡPsPrCḡPeC,PḡPIPSPsPiPs PIC-PeCḡ CḡP»C-Pr
CḡPḡPePsPjPḡPSPPrCḡPIP°C,Pḡ PIPḡPePsCḡPḡCḡC,PsPICḡPIP°C,Pḡ PSP°P»PḡPḡPSC-
P·P°CḡPsP±Pḡ PePsPSC,CḡP°C†PḡPiC†C-C— PiC-Pr CḡP°Cḡ C,PḡCḡP°PiC-C—
C,PsC,,P°C†PḡC,PḡPSC-P±PsPj C- PḡCḡPsC,CḡPiPsPj CḡḡPsPSP°PNḡPjPḡPSCḡPḡ 4 C,PḡPḡPSC-PI
PiC-CḡP»Cḡ PḡCḡPḡPNḡPjP°PSPSCḡ PsCḡC,P°PSPSCḡPsC— PrPsP·Pḡ.

P"PsPrCḡPIP°PSPSCḡ PiCḡCḡPrPrCḡ

PḡPḡPIC-PrPsPjPs, CḡPḡ PIPḡPrC-P»CḡC"C,CHCḡCḡ C,PsC,,P°C†PḡC,PḡPSC-P± C-P·
PiCḡCḡPrPSPḡPj PjPsP»PsPePsPj Cḡ P»CHPrPḡPSPḡ. PḡPḡ PjPsPḡPSP° PIPḡPeP»CHCḡPḡC,Pḡ
CḡPḡP·PḡPe PrP»Cḡ PSPḡPjPsPIP»CḡC,Pḡ, CḡḡPs PḡPḡCḡPḡP±CḡPIP°C" PSP° PiCḡCḡPrPSPsPjCḡ
PIPḡPiPsPrPsPICḡPIP°PSPSC-. PḡPsC,,P°C†PḡC,PḡPSC-P± PIPḡPrC-P»CḡPICḡCḡ
P· PjPsP»PsPePsPj Cḡ CḡḡCḡCḡC-PI Cḡ PḡPḡCḡC-PsPr P»P°PeC,P°C†C-C—. PḡPe
P·P°PḡPsP±C-PḡPSPḡPNḡ P·P°C...C-Pr, P·P°CḡC,PsCḡCḡPIP°PSPSCḡ C,PsC,,P°C†PḡC,PḡPSC-P±Cḡ
PiC-Pr CḡP°Cḡ PiPsPrCḡPIP°PSPSCḡ PiCḡCḡPrPrCḡ PḡCḡPsC,PḡPḡPsPeP°P·P°PSPs (PrPḡPI.
CḡPsP·PrC-P» B«PḡCḡPsC,PḡPḡPsPeP°P·P°PSPSCḡB»).

P PḡPiCḡPsPrCḡPeC,PḡPIPSP° C,,CḡPSPeC†C-Cḡ

PḡPsCḡPjP°P»CHPSPḡC... PrPsCḡP»C-PrPḡPḡPSCḡ PḡPsC,PḡPSC†C-P°P»Cḡ PIPḡP»PḡPICḡ
C†CHPsPiPs P»C-PeP°CḡCḡCHPePsPiPs P·P°CḡPsP±Cḡ PSP° C,,PḡCḡC,PḡP»CHPSC-CḡC,CH
Cḡ P»CHPrPḡPSPḡ PSPḡ PḡCḡPsPIPPrPḡP»PsCḡCḡ. Pj CḡḡCḡCḡC-PI C,PsC,,P°C†PḡC,PḡPSC-P±
CḡPiCḡPḡCḡPḡPSCḡPI PḡPsCḡCḡCḡPḡPSPSCḡ C,,PḡCḡC,PḡP»CHPSPsCḡC,C- PI CḡP°PjPsPe,
P°P»Pḡ PSPḡ PI CḡP°PjC†C-PI.

***P—PrP°C,PSC—CÍC,CH PIPiP»PëPIP°C,Pë PSP° C€PIPëPrPeC—CÍC,CH CḡPμP°PeC†C—
PİCḡPë PePμCḡC¿PIP°PSPSC- P°PIC,PsC,CḡP°PSCÍPİPsCḡC,PsPj P°P±Ps C-PSC€PëPjPë
PjPμC...P°PSC-P·PjP°PjPë.***

PŷPsC,,P°C†PëC,PëPSC—P± PSPμ PIPiP»PëPIP°C” P°P±Ps PjP°PNëP¶Pμ PSPμ PIPiP»PëPIP°C” PSP°
P·PrP°C,PSC—CÍC,CH PePμCḡCÍPİP°C,Pë C,CḡP°PSCÍPİPsCḡC,PSPëPjPë P·P°CÍPsP±P°PjPë C,P°
PİCḡP°C†CḡPIP°C,Pë P· C—PSC€PëPjPë PjPμC...P°PSC—P·PjP°PjPë.

PŷPİPsCÍC—P± P·P°CÍC,PsCÍC¿PIP°PSPSCİ C,P° PrPsP·Pë.

P PsP·PİPsC±PëPSP°C,Pë PNë PİCḡPsPIPİPrPëC,Pë C,PμCḡP°PİC—Cḡ CÍP»C—Pr PİC—Pr
PePsPSC,CḡPsP»PμPj PjPμPrPëC±PSPİPs PİCḡP°C†C—PİPSPëPeP° P· PrPsCÍPIC—PrPsPj
PrC—P°PİPSPİCÍC,CÍPİP°PSPSCİ C,P° P»C—PeCÍPİP°PSPSCİ P·P°C...PIPİCḡCḡPIP°PSCḡ,
PrP»Cİ P»C—PeCÍPİP°PSPSCİ CİPePëC... PİCḡPëP·PSP°C±PμPSPëPNë C,PsC,,P°C†PëC,PëPSC—P±.

P”PsP·Pë

P PμPIPjP°C,PsC—PrPSPëPNë P°CḡC,CḡPëC, C— PİCÍPsCḡC—P°C,PëC±PSPëPNë P°CḡC,CḡPëC.

P PμPePsPjPμPSPPrPsPIP°PSP° PrPsP·P° CÍC,P°PSPİPİPëC,CH PİPs PsPrPSC—PNë
C,P°P±P»PμC,C†C—, PİPeCḡPëC,C—PNë PİP»C—PİPePsPIPİCḡ PsP±PsP»PsPSPİPsCḡ, 5 PjPİ PrPIP°
CḡP°P·Pë PSP° PrPsP±CÍ C°oPsPrPμPSPSPİ; C†Cḡ PrPsP·CÍ PSPμ PjPsP¶PSP°
PİPμCḡPμPIPëC°oCÍPİP°C,Pë.

Pj CḡP°P·C— P·P°CÍC,PsCÍCÍPİP°PSPSCİ Pİ PePsPjP±C—PSP°C†C—C— P· MTX
PePsCḡPμPeC†C—Cİ PrPsP·Pë PSPμ PİPsC,CḡC—P±PSP°.

PḡPSPİC—P»PsP·C¿CḡC±PëPNë CÍPİPsPSPPrPëP»C—C.

P PμPePsPjPμPSPPrPsPIP°PSP° PrPsP·P° C,PsC,,P°C†PëC,PëPSC—P±CÍ CÍC,P°PSPİPİPëC,CH 5 PjPİ
PrPIP° CḡP°P·Pë PSP° PrPsP±CÍ.

P’PëCḡP°P·PePsPIPëPNë PePsP»C—C.

P†PSPrC¿PeC†C—PNëPSP° C,PμCḡP°PİC—Cİ

P”P»Cİ C—PSPrCÍPeCÍPİP°PSPSCİ PIC—PrPİPsPIC—PrC— CḡPμPePsPjPμPSPPrPsPIP°PSP° PrPsP·P°
CÍC,P°PSPİPİPëC,CH 10 PjPİ PİPμCḡPsCḡP°P»CHPSPİ PrPIP° CḡP°P·Pë PSP° PrPsP±CÍ
PİCḡPsC,CİPİPsPj 8 C,PëP¶PSC—Pİ.

PμP°C†C—C”PSC,P°Pj, CÍ CİPePëC... PSPμ CÍPİPsCÍC,PμCḡC—PİP°C”C,CHCÍCİ PSP°P»PμP¶PSP°
C,PμCḡP°PİPμPIC,PëC±PSP° PIC—PrPİPsPIC—PrCH PrPs 8—PİPs C,PëP¶PSCİ,
C—PSPrCÍPeC†C—PNëPSCÍ PrPsP·CÍ 10 PjPİ PrPIP° CḡP°P·Pë PSP° PrPsP±CÍ PjPsP¶PSP°
PİPsPrPsPIP¶PëC,Pë C°oPμ PSP° 8 C,PëP¶PSC—Pİ (C,PsP±C,Ps P·P°PİP°P»PsPj 16 C,PëP¶PSC—Pİ),
P° PİPsC,C—Pj P·P°CÍC,PsCÍPsPICÍCḡC,CH PrPsP·CÍ 5 PjPİ PrPIP° CḡP°P·Pë PSP° PrPsP±CÍ
CİPe PİC—PrC,CḡPëPjCÍPİP°P»CHPSCÍ C,PμCḡP°PİC—Cḡ. P’CÍPrCH—CİPePsPjCÍ
PİP°C†C—C”PSC,PsPIC—, CÍ CİPePsPİPs PrPs C,PëP¶PSCİ 16 PSPμ P·ḡḡ™ CİPİPëP»PëCÍCİ
PsP·PSP°PePë PİPsP·PëC,PëPİPSPİPs C,PμCḡP°PİPμPIC,PëC±PSPİPs PμC,,PμPeC,CÍ,
C—PSPrCÍPeC†C—PNëPSCÍ C,PμCḡP°PİC—Cḡ C,PsC,,P°C†PëC,PëPSC—P±PsPj CÍP»C—Pr
PİCḡPëPİPëPSPëC,Pë.

P_μC-PrC,CTHPēPjCáPIP°P»CHBPSP° C,P_μCTHP°PīC-ClI

P P_μPePsPjP_μPSPPrPsPIP°PSP° PrPsP·P° C,PsC,,P°C†PēC,PēPSC-P±Cf ClI_{Pe}
PīC-PrC,CTHPēPjCfPIP°P»CHBPSPsC— C,P_μCTHP°PīC-C— ClfC,P°PSPsPIPēC,CH 5 PjPi
PīP_μCTHPsCTHP°P»CHBPSPs PrPIP° CTHP°P·Pē PSP° PrPsP±Cf.

PŷPsC,,P°C†PēC,PēPSC-P± Cf PrPsP·C- 10 PjPi PrPIP° CTHP°P·Pē PSP° PrPsP±Cf PrP»ClI
PīC-PrC,CTHPēPjCfPIP°P»CHBPSPsC— C,P_μCTHP°PīC-C— PSP_μ CTHP_μPePsPjP_μPSPPrCfC”C,CHClfClI
P·P°ClfC,PsClfPsPICfPIP°C,Pē PīP°C†C-C”PSC,P°Pj C-P· P’P_л, Cf ClI_{Pe}PēC... C” PIC-PrPsPjC-
C,,P°PeC,PsCTHPē CTHPēP·PēPeCf PIP_μPSPsP·PSPsC— C,CTHPsPjP±PsP_μPjP±PsP»C-C— (P’PŷP·),
ClfP_μCTHPN_μPsP·PSPēC... PSP_μClfPīCTHPēClI_C,P»PēPIPēC... ClfP_μCTHC†P_μPIPs-ClfCfPrPēPSPSPēC...
PīPsPrC-PN_μ (MACE) C,P° C,,P°PeC,PsCTHPē CTHPēP·PēPeCf CTHPsP·PIPēC,PeCf
P·P»PsClI_{Pe}C-ClfPSPēC... PSPsPIPsCfC,PIPsCTHP_μPSCH, P·P° PIPēPSClI_C,PePsPj
PIPēPīP°PrPeC-PI, PePsP»Pē PSP_μPjP°C” P°P»CHC,P_μCTHPSP°C,PēPIPSPēC... PjP_μC,PsPrC-PI
P»C-PeCfPIP°PSPSClI (PrPēPI. CTHPsP·PrC-P»Pē B«PhClfPsP±P»PēPIPsClfC,C-
P·P°ClfC,PsClfCfPIP°PSPSClIB» C- B«P_μPsP±C-C†PSC- CTHP_μP°PeC†C-C—B»).

P”P»ClI PīP°C†C-C”PSC,C-PI C-P· P’P_л, Cf ClI_{Pe}PēC... PSP_μPjP°C” PīC-PrPIPēC%_μP_μPSPsPiPs
CTHPēP·PēPeCf CTHPsP·PIPēC,PeCf P’PŷP·, P_лP_лPŷP· C,P° P·P»PsClI_{Pe}C-ClfPSPēC...
PSPsPIPsCfC,PIPsCTHP_μPSCH (PrPēPI. CTHPsP·PrC-P» B«PhClfPsP±P»PēPIPsClfC,C-
P·P°ClfC,PsClfCfPIP°PSPSClIB»), PjPsP_μPSP° CTHPsP·PiP»ClIPSCfC,Pē PjPsP_μP»PēPIC-ClfC,CH
P·P°ClfC,PsClfCfPIP°PSPSClI C,PsC,,P°C†PēC,PēPSC-P±Cf PI PrPsP·C- 10 PjPi
PīP_μCTHPsCTHP°P»CHBPSPs PrPIP° CTHP°P·Pē PSP° PrPsP±Cf, ClI_{Pe}C%_μPs PI PīP°C†C-C”PSC,P°
ClfPīPsClfC,P_μCTHC-PiP°P»PsClfClI P·PSPēP_μPSPSClI PIC-PrPīPsPIC-PrC- PSP°
C,PsC,,P°C†PēC,PēPSC-P± Cf PrPsP·C- 5 PjPi PrPIP° CTHP°P·Pē PSP° PrPsP±Cf PN_μ PSP_μ P±CfP»Ps
PIC-PrPīPsPIC-PrC- PSP° P°P»CHC,P_μCTHPSP°C,PēPIPSC- PīCTHP_μPīP°CTHP°C,Pē PrP»ClI
P»C-PeCfPIP°PSPSClI PIPēCTHP°P·PePsPIPsPiPs PePsP»C-C,Cf, ClI_{Pe}-PsC,
C-PSPiC-P±C-C,PsCTHPē C,,P°PeC,PsCTHP° PSP_μPeCTHPsP·Cf PīCfC...P»PēPSPē
(C-PSPiC-P±C-C,PsCTHPē P_μP_лP_μ). PŷPsC,,P°C†PēC,PēPSC-P± Cf PrPsP·C- 10 PjPi PrPIP°
CTHP°P·Pē PSP° PrPsP±Cf ClI_{Pe} PīC-PrC,CTHPēPjCfPIP°P»CHBPSCf C,P_μCTHP°PīC-CH ClfP»C-Pr
P·P°ClfC,PsClfPsPICfPIP°C,Pē PīCTHPsC,ClIPiPsPj PSP°PN_μPePsCTHPsC,CfPsPiPs
PjPsP_μP»PēPIPsPiPs PīP_μCTHC-PsPrCf. PŷP»C-Pr P·P°ClfC,PsClfPsPICfPIP°C,Pē
PSP°PN_μPSPēP_μC†Cf P_μC,,P_μPeC,PēPIPSCf PrPsP·Cf, PīPsC,CTHC-P±PSCf PrP»ClI
PīC-PrC,CTHPēPjP°PSPSClI PIC-PrPīPsPIC-PrC-.

P_μP°C†C-C”PSC,P°Pj, ClI_{Pe}C- PIC-PrPīPsPIC-P»Pē PSP° C,P_μCTHP°PīC-CH
C,PsC,,P°C†PēC,PēPSC-P±PsPj, PrPsP·Cf PePsCTHC,PēPePsClfC,P_μCTHPsC—PrC-PI PjPsP_μPSP°
P·PjP_μPSCfPēC,Pē C,P°/P°P±Ps PīCTHPēPīPēPSPēC,Pē P·P°ClfC,PsClfCfPIP°PSPSClI
PePsCTHC,PēPePsClfC,P_μCTHPsC—PrC-PI PIC-PrPīPsPIC-PrPSPs PrPs ClfC,P°PSPPrP°CTHC,C-PI
P»C-PeCfPIP°PSPSClI.

P_μPsPSPsPIP»P_μPSPSClI C,P_μCTHP°PīC-C— PīCTHPē P’P_л

PīPeC%_μPs C,P_μCTHP°PīC-CH P±CfP»Ps PīP_μCTHP_μCTHIP°PSPs, PjPsP_μPSP°
CTHPsP·PiP»ClIPSCfC,Pē PjPsP_μP»PēPIC-ClfC,CH PīPsPSPsPIP»P_μPSPSClI P»C-PeCfPIP°PSPSClI
C,PsC,,P°C†PēC,PēPSC-P±PsPj. PīPeC%_μPs ClfPīPsClfC,P_μCTHC-PiP°P»P°ClfClI PIC,CTHP°C,P°
PIC-PrPīPsPIC-PrC-, PjPsP_μPSP° CTHPsP·PiP»ClIPSCfC,Pē PrPsC†C-P»CHBPSC-ClfC,CH
PīPsPIC,PsCTHPSPsPiPs PeCfCTHCfCf C-PSPrCfPeC†C-PN_μPSPsC— C,P_μCTHP°PīC-C—
C,PsC,,P°C†PēC,PēPSC-P±PsPj Cf PrPsP·C- 10 PjPi PrPIP° CTHP°P·Pē PSP° PrPsP±Cf.
P_μP_μCTHC-PsPr, PSP° ClI_{Pe}PēPN_μ PīCTHPēP·CfPīPēPSClI»Pē C,P_μCTHP°PīC-CH PI
PeP»C-PSC-C†PSPēC... PrPsClfP»C-PrP_μPSPSClI..., C,CTHPēPIP°PI PrPs 1 CTHPsPeCf.
P·C,,P_μPeC,PēPIPSC-ClfC,CH PjPsP_μP_μ P±CfC,Pē PIC-PrPSPsPIP»P_μPSP° C†P_μCTHP_μP·

8 C,PëP¶PSC-PI C,PµCḡP°PīC-C— PI PrPsP·C- 10 PjPi PrPIP° CḡP°P·Pë PSP° PrPsP±Cf.

PµPsP»C-P°CḡC,PëPeCḡP»CḡCḡPSPëPNḡ P®P†Pḡ (PrC-C,Pë P· PjP°CḡPsCḡ C,C-P»P° ≥ 40 PePi)

PŷPsC,,P°C†PëC,PëPSC-P± PjPsP¶PSP° P·P°CḡC,PsCḡPsPICfPIP°C,Pë CḡPe
PjPsPSPsC,PµCḡP°PīC-Cḡ P°P±Ps PI PePsPjP±C-PSP°C†C-C— P· MTX.

P PµPePsPjPµPSPPrPsPIP°PSP° PrPsP·P° C,PsC,,P°C†PëC,PëPSC-P±Cf PI P»C-PeP°CḡCḡPëC-PNḡ
C,,PsCḡPjC- C,P°P±P»PµC,PePë, PIPeCḡPëC,C- PīP»C-PIPePsPIPsCḡ PsP±PsP»PsPSPePsCḡ,
PrP»Cḡ PīP°C†C-C”PSC,C-PI PrPëC,CḡC†PsPiPs PIC-PeCf P· PjP°CḡPsCḡ C,C-P»P° ≥ 40 PePi
CḡC,P°PSPsPIPëC,Cḡ 5 PjPi PrPIP° CḡP°P·Pë PSP° PrPsP±Cf.

PµP°C†C-C”PSC,P°Pj PrPëC,CḡC†PsPiPs PIC-PeCf C-P· PjP°CḡPsCḡ C,C-P»P° < 40 PePi CḡP»C-Pr
P·P°CḡC,PsCḡPsPICfPIP°C,Pë C-PSC€C- P»C-PeP°CḡCḡPëC- C,,PsCḡPjPë
C,PsC,,P°C†PëC,PëPSC-P±Cf (CḡPsP·C†PëPS PrP»Cḡ PīPµCḡPsCḡP°P»CḡPSPsPiPs
P·P°CḡC,PsCḡCfPIP°PSPSCḡ).

PŷPëPjC†P°CḡPsPIPµ PīCḡPëP·CfPīPëPSPµPSPSCḡ C,P° PīPsPIPSPµ PīCḡPëPīPëPSPµPSPSCḡ
P·P°CḡC,PsCḡCfPIP°PSPSCḡ PīCḡPµPīP°CḡP°C,Cf PrPsCḡPsCḡP»PëPj C- PrC-C,CḡPj

PīPeC%oPs PI PīP°C†C-C”PSC,P° PIPëPSPëPeP»P° CḡPµCḡPNḡPsP·PSP° C-PSC,,PµPeC†C-Cḡ,
C,PµCḡP°PīC-Cḡ C,PsC,,P°C†PëC,PëPSC-P±PsPj CḡP»C-Pr C,PëPjC†P°CḡPsPIPs
PīCḡPëP·CfPīPëPSPëC,Pë, PrPsPePë PSPµ P±CfPrPµ PrPsCḡCḡPiPSCfC,PëPNḡ
PePsPSC,CḡPsP»Cḡ C-PSC,,PµPeC†C-C—.

PµCḡPëP·CfPīPëPSPµPSPSCḡ PrPsP·CfPIP°PSPSCḡ PjPsP¶Pµ P±CfC,Pë PīPsC,CḡC-P±PSPµ
PrP»Cḡ P»C-PeCfPIP°PSPSCḡ PrPsP·PsP·P°P»PµP¶PSPëC... PIC-PrC...PëP»PµPSCḡ PIC-Pr
PSPsCḡPjPë P·P° CḡPµP·CfP»CḡC,P°C,P°PjPë P»P°P±PsCḡP°C,PsCḡPSPëC... P°PSP°P»C-P·C-PI,
P·PsPeCḡPµPjP° P»C-PjC,,PsPīPµPSC-C—, PSPµPNḡC,CḡPsPīPµPSC-C— C,P° P°PSPµPjC-C—. PīPe
PīPsPeP°P·P°PSPs PI C,P°P±P»PëC†CḡC... 1, 2 C- 3 PSPëP¶C†Pµ, CḡPµPePsPjPµPSPPrP°C†C-C—
C%oPsPrPs C,PëPjC†P°CḡPsPIPsPīPs PīCḡPëP·CfPīPëPSPµPSPSCḡ P·P°CḡC,PsCḡCfPIP°PSPSCḡ
P»C-PeP°CḡCḡPëPsPiPs P·P°CḡPsP±Cf P°P±Ps PsCḡC,P°C,PsC†PSPsPiPs
PīCḡPëPīPëPSPµPSPSCḡ C,PµCḡP°PīC-C— P·P°P»PµP¶P°C,Cḡ PIC-Pr CḡC,CfPīPµPSCḡ
C,CḡP¶PePsCḡC,C- PIC-PrC...PëP»PµPSCḡ PIC-Pr PSPsCḡPjPë P·P° CḡPµP·CfP»CḡC,P°C,P°PjPë
P»P°P±PsCḡP°C,PsCḡPSPëC... P°PSP°P»C-P·C-PI (PrPëPI.
CḡPsP·PrC-P» B«PhCḡPsP±P»PëPIPsCḡC,C- P·P°CḡC,PsCḡCfPIP°PSPSCḡB»).

P PµPePsPjPµPSPPrCfC”C,CḡCḡCḡ PSPµ PīPsC†PëPSP°C,Pë PrPsP·CfPIP°PSPSCḡ
PīCḡPµPīP°CḡP°C,Cf PīP°C†C-C”PSC,P°Pj, Cf CḡPePëC... P°P±CḡPsP»CḡC,PSP°
PeC-P»CḡPeC-CḡC,Cḡ P»C-PjC,,PsC†PëC,C-PI (PḡPḡP) CḡC,P°PSPsPIPëC,Cḡ PjPµPSC€Pµ
750 PeP»C-C,PëPS/PjPj³.

PŷP°P±P»PëC†Cḡ 1. PkPëP·CḡPeP° P°P±CḡPsP»CḡC,PSP° PeC-P»CḡPeC-CḡC,Cḡ
P»C-PjC,,PsC†PëC,C-PI

PkPëP·CḡPeP° P°P±CḡPsP»CḡC,PSP° PeC-P»CḡPeC-CḡC,Cḡ P»C-PjC,,PsC†PëC,C-PI (PḡPḡP) (PrPëPI. CḡPsP·PrC-P» B«PhCḡPsP±P»PëPIPsCḡC,C- P·P°CḡC,PsCḡCfPIP°PSPSCḡB»)	
P»P°P±PsCḡP°C,PsCḡPSPµ P·PSP°C†PµPSPSCḡ (PeP»C-C,PëPS/PjPj ³)	PµPePsPjPµPSPPrP°C†C-C—
PḡPḡP PīPsPSP°Pr P°P±Ps PrPsCḡC-PIPSCHC” 750	P”PsP·Cf CḡP»C-Pr P·P°P»PëC€PëC,Pë PSP° PīPsC,PsC†PSPsPjCf CḡC-PIPSCHC—.

PhPbPá 500Bh“1000	PJ CĤP°P·C- CĤC,C-PN₂PePsPiPs P·PSPëP¶PµPSPSCĬ PĭPsPeP°P·PSPëPeP° Cŕ P·P°P·PSP°C‡PµPSPsPjCŕ PrC-P°PĭP°P·PsPSC- (2 CĤP°P·Pë PĭPsCĬPĭC-P»CH PĭC-Pr C‡P°CĬ CĤCŕC,PëPSPSPsPiPs C,PµCĬC,CŕPIP°PSPSCĬ) CĬP»C-Pr P·PjPµPSCëPëC,Pë PrPsP·Cŕ P°P±Ps PĭCĤPëP·CŕPĭPëPSPëC,Pë C,PµCĤP°PĭC-CH. PµP°C‡C-C”PSC,P°Pj, CĬPeC- PsC,CĤPëPjCŕCHC,CH C,PsC,,P°C‡PëC,PëPSC-P± Cŕ PrPsP·C- 10 PjPi PrPIP° CĤP°P·Pë PSP° PrPsP±Cŕ, PrPsP·Cŕ CĬP»C-Pr P·PjPµPSCëPëC,Pë PrPs 5 PjPi C,PsC,,P°C‡PëC,PëPSC-P±Cŕ PrPIP° CĤP°P·Pë PSP° PrPsP±Cŕ. PµP°C‡C-C”PSC,P°Pj, CĬPeC- PsC,CĤPëPjCŕCHC,CH C,PsC,,P°C‡PëC,PëPSC-P± Cŕ PrPsP·C- 5 PjPi PrPIP° CĤP°P·Pë PSP° PrPsP±Cŕ, P·P°CĬC,PsCĬCŕPIP°PSPSCĬ PĭCĤPµPĭP°CĤP°C,Cŕ CĬP»C-Pr PĭCĤPëP·CŕPĭPëPSPëC,Pë. PµPsP»Pë PhPbPá PĭPµCĤPµPIPëC‰PëC,CH P·PSP°C‡PµPSPSCĬ 1000 PeP»C-C,PëPS, C,PµCĤP°PĭC-CH CĬP»C-Pr PĭPsPSPsPIPëC,Pë P· CŕCĤP°C...CŕPIP°PSPSCĬPj PeP»C-PSC-C‡PSPsC— PeP°CĤC,PëPSPë.
PhPbPá PjPµPSCëPµ 500	PĭPeC‰Ps C,P°PePµ P»P°P±PsCĤP°C,PsCĤPSPµ P·PSP°C‡PµPSPSCĬ PĭC-PrC,PIPµCĤPPrP¶CŕC”C,CHCĬCĬ PĭPsPIC,PsCĤPSPëPj C,PµCĬC,CŕPIP°PSPSCĬPj, PIPëPePsPSP°PSPëPj PĭCĤPsC,CĬPiPsPj 7 PrPSC-PI PĭC-CĬP»CĬ PĭPsPĭPµCĤPµPrPSCĤPsPiPs P°PSP°P»C-P·Cŕ, C,PµCĤP°PĭC-CH PĭCĤPµPĭP°CĤP°C,PsPj PµCĬPµP»CHCĬPSP· CĬP»C-Pr PĭCĤPëPĭPëPSPëC,Pë.

P PµPePsPjPµPSPŕCŕC”C,CHCĬCĬ PSPµ PĭPsC‡PëPSP°C,Pë C,PµCĤP°PĭC-CH PrPsCĤPsCĬP»PëPj
PĭP°C‡C-C”PSC,P°Pj, Cŕ CĬPePëC... CĤC-PIPµPSCĤ PĭPµPjPsPiP»PsP±C-PSCŕ
CĬC,P°PSPsPIPëC,CH PSPëP¶C‡Pµ 9 Pi/PrP». P PµPePsPjPµPSPŕCŕC”C,CHCĬCĬ PSPµ
PĭPsC‡PëPSP°C,Pë C,PµCĤP°PĭC-CH PrC-C,CĬPj, Cŕ CĬPePëC... CĤC-PIPµPSCĤ
PĭPµPjPsPiP»PsP±C-PSCŕ CĬC,P°PSPsPIPëC,CH PSPëP¶C‡Pµ 10 Pi/PrP».

PŷP°P±P»PëC‡CĬ 3. PáPëP·CHPePëPN₂ CĤC-PIPµPSCĤ PĭPµPjPsPiP»PsP±C-PSCŕ

PáPëP·CHPePëPN ₂ CĤC-PIPµPSCĤ PĭPµPjPsPiP»PsP±C-PSCŕ (PrPëPI. CĤPsP·PrC-P» B«PhCĬPsP±P»PëPIPsCĬC,C- P·P°CĬC,PsCĬCŕPIP°PSPSCĬB»)	
P·P°P±PsCĤP°C,PsCĤPSPµ P·PSP°C‡PµPSPSCĬ (Pi/PrP»)	P PµPePsPjPµPSPŕP°C‡C-C—
P C-PIPµPSCĤ P·PSPëP¶CŕC”C,CHCĬCĬ PSPµ P±C-P»CHCëPµ PSC-P¶ PSP° 2 Pi/PrP» C- CĬC,P°PSPsPIPëC,CH PSPµ PjPµPSCëPµ 9,0 Pi/PrP»	P”PsP·Cŕ CĬP»C-Pr P·P°P»PëCëPëC,Pë PSP° PĭPsC,PsC‡PSPsPjCŕ CĤC-PIPSC-.
P C-PIPµPSCĤ P·PSPëP¶CŕC”C,CHCĬCĬ P±C-P»CHCëPµ PSC-P¶ PSP° 2 Pi/PrP» P°P±Ps CĬC,P°PSPsPIPëC,CH PjPµPSCëPµ 8,0 Pi/PrP» (C‰Ps PĭC-PrC,PIPµCĤPPrP¶CŕC”C,CHCĬCĬ PĭPsPIC,PsCĤPSPëPj C,PµCĬC,CŕPIP°PSPSCĬPj)	P”PsP·CŕPIP°PSPSCĬ CĬP»C-Pr PĭCĤPëP·CŕPĭPëPSPëC,Pë, PrPsPePë CĤC-PIPµPSCĤ PĭPµPjPsPiP»PsP±C-PSCŕ PSPµ PSPsCĤPjP°P»C-P·CŕC”C,CHCĬCĬ.

P’P·P°C”PjPsPrC-C—

P—P°PĭP°P»CHPSCŕ PrPsP±PsPICŕ PrPsP·Cŕ C,PsC,,P°C‡PëC,PëPSC-P±Cŕ CĬP»C-Pr
P·PjPµPSCëPëC,Pë PIPŕPIC-C‡C- PĭP°C‡C-C”PSC,P°Pj, CĬPeC- PsC,CĤPëPjCŕCHC,CH
PĭPsC,CŕP¶PSC- C-PSPiC-P±C-C,PsCĤPë C-P·PsC,,PµCĤPjPµPSC,Cŕ 3A4 CĬPëCĬC,PµPjPë
C‡PëC,PsC...CĤPsPjCŕ P450 (CYP) (PSP°PĭCĤPëPeP»P°Pr, PePµC,PsPePsPSP°P·PsP»), P°

C,P°PePsP¶ PiP°C†C-C"°PSC,P°Pj, C¶PeC- PsPrPSPsC†P°C†PSPs PsC,C¶PëPjC†C¶C,C¶ 1 P°P±Ps PeC-P»C¶PeP° P»C-PeP°C¶C†C¶PePëC... P·P°C†PsP±C-PI, C°°Ps C†PiC¶PëC†PëPSC¶C¶C,C¶ C¶Pe PiPsPjC-C¶PSPµ C-PSPiC-P±C†PIP°PSPSC¶ CYP3A4, C,P°Pe C- PiPsC,C†P¶PSPµ C-PSPiC-P±C†PIP°PSPSC¶ CYP2C19 (PSP°PiC¶PëPeP»P°Pr, C,,P»C†PePsPSP°P·PsP») (PrPëPI. C¶PsP·PrC-P» B«P·P·P°C"°PjPsPrC-C¶ P· C-PSC¶PëPjPë P»C-PeP°C¶C†C¶PePëPjPë P·P°C†PsP±P°PjPë C,P° C-PSC¶C- PIPëPrPë PIP·P°C"°PjPsPrC-PNëB»), P° C†P°PjPµ:

B· P°PsP·C† C,PsC,,P°C†PëC,PëPSC-P±C† C†P»C-Pr P·PjPµPSC¶PëC,Pë PrPs 5 PjPi PsPrPëPS C¶P°P· PSP° PrPsP±C† PiP°C†C-C"°PSC,P°Pj, C¶PeC- PsC,C¶PëPjC†C¶C,C¶ PrPsP·C† 5 PjPi PrPIP° C¶P°P·Pë PSP° PrPsP±C† (C†Pµ C†C,PsC†C†C"°C,C¶C†C¶ C- PrPsC¶PsC†P»PëC..., C- PrC-C,PµPNë).

B· P°PsP·C† C,PsC,,P°C†PëC,PëPSC-P±C† C†P»C-Pr P·PjPµPSC¶PëC,Pë PrPs 5 PjPi PrPIP° C¶P°P·Pë PSP° PrPsP±C† PiP°C†C-C"°PSC,P°Pj, C¶PeC- PsC,C¶PëPjC†C¶C,C¶ PrPsP·C† 10 PjPi PrPIP° C¶P°P·Pë PSP° PrPsP±C† (PrPsC¶PsC†P»PëPj PiP°C†C-C"°PSC,P°Pj).

PŸC,PsC†C†C"°C,C¶C†C¶ C,C-P»C¶PePë PrC-C,PµPNë: PSP°C¶PIPSC- PrP°PSC- C†PIC-PrC†P°C,C¶ PiC¶Ps C,Pµ, C°°Ps PeP»C-PSC-C†PSPµ PiPsPeC¶P°C°°PµPSPSC¶ C†PiPsC†C,PµC¶C-PiP°C"°C,C¶C†C¶ PiC¶PsC,C¶PiPsPj 18 C,PëP¶PSC-PI PiC-C†P»C¶ PiPsC†P°C,PeC† C,PµC¶P°PiC-C— C,PsC,,P°C†PëC,PëPSC-P±PsPj. P"°P»C¶ PiP°C†C-C"°PSC,C-PI, C† C¶PePëC... PiC¶PsC,C¶PiPsPj C†C¶PsPiPs PiPµC¶C-PsPrC† PSPµ C†PiPsC†C,PµC¶C-PiP°C"°C,C¶C†C¶ PeP»C-PSC-C†PSPsPiPs PiPsPeC¶P°C°°PµPSPSC¶, C†P»C-Pr C¶PsP·PiP»C¶PSC†C,Pë PrPsC†C-P»C¶PSC-C†C,C¶ PiC¶PsPrPsPIP¶PµPSPSC¶ C,PµC¶P°PiC-C—, P°P»Pµ P· C¶PµC,PµP»C¶PSPëPj P·PIP°P¶C†PIP°PSPSC¶Pj C†C†C-C... PiPµC¶PµPIP°Pi C- C¶PëP·PëPeC-PI.

PµC¶PëPiPëPSPµPSPSC¶ C,PµC¶P°PiC-C— PiC¶Pë P°PSPeC-P»PsP·C†C¶C†PsPjC† C†PiPsPSPPrPëP»C-C,C-

P°P°C¶PIPSC- PrP°PSC- C†PIC-PrC†P°C,C¶ PiC¶Ps C,Pµ, C°°Ps PeP»C-PSC-C†PSPµ PiPsPeC¶P°C°°PµPSPSC¶ PiC¶Pë P¶PŸ C†PiPsC†C,PµC¶C-PiP°C"°C,C¶C†C¶ PiC¶PsC,C¶PiPsPj 16 C,PëP¶PSC-PI PiC-C†P»C¶ PiPsC†P°C,PeC† C,PµC¶P°PiC-C— C,PsC,,P°C†PëC,PëPSC-P±PsPj. P"°P»C¶ PiP°C†C-C"°PSC,C-PI, C† C¶PePëC... PiC¶PsC,C¶PiPsPj C†C¶PsPiPs PiPµC¶C-PsPrC† PSPµ C†PiPsC†C,PµC¶C-PiP°C"°C,C¶C†C¶ PeP»C-PSC-C†PSPsPiPs PiPsPeC¶P°C°°PµPSPSC¶, C†P»C-Pr C¶PsP·PiP»C¶PSC†C,Pë PrPsC†C-P»C¶PSC-C†C,C¶ PiC¶PsPrPsPIP¶PµPSPSC¶ C,PµC¶P°PiC-C—, P°P»Pµ P· C¶PµC,PµP»C¶PSPëPj P·PIP°P¶C†PIP°PSPSC¶Pj C†C†C-C... PiPµC¶PµPIP°Pi C- C¶PëP·PëPeC-PI.

P¶C†PsP±P»PëPIC- PiC¶C†PiPë PiP°C†C-C"°PSC,C-PI

PµP°C†C-C"°PSC,Pë PiPsC...PëP»PsPiPs PIC-PeCž

PµP°C†C-C"°PSC,P°Pj PIC-PePsPj 65 C¶PsPeC-PI C- C†C,P°C¶C¶Pµ PePsC¶PµPeC†C-C¶ PrPsP·Pë PSPµ PiPsC,C¶C-P±PSP°. P"°P°PSC- C°°PsPrPs P·P°C†C,PsC†C†PIP°PSPSC¶ PiC¶PµPiP°C¶P°C,C† PiP°C†C-C"°PSC,P°Pj PIC-PePsPj C†C,P°C¶C¶Pµ 75 C¶PsPeC-PI PSP°C¶P°P·C- PsP±PjPµP¶PµPSC-. P PµPePsPjPµPSPPrP°C†C-C— C°°PsPrPs P·P°C†C,PsC†C†PIP°PSPSC¶ PiP°C†C-C"°PSC,P°Pj PIC-PePsPj 65 C¶PsPeC-PI C- C†C,P°C¶C¶Pµ PrPëPI. C† C¶PsP·PrC-P»C- B«P¶C†PsP±P»PëPiPsC†C,C- P·P°C†C,PsC†C†PIP°PSPSC¶B».

PµPµC†C-PSPePsPIP° PSPµPrPsC†C,P°C,PSC-C†C,C¶

PŸP°P±P»PëC†C¶ 4. P¶PsC¶PµPeC†C-C¶ PrPsP·Pë PiC¶Pë PiPµC†C-PSPePsPIC-PNë PSPµPrPsC†C,P°C,PSPsC†C,C-

PIC-PrCfCfC,PSC-.

P'PμP·PiPμPeP° C,P° PμC,,PμPeC,PēPIPSC-CfC,CH P·P°CfC,PsCfCfPIP°PSPSCl
C,PsC,,P°C†PēC,PēPSC-P±Cf PrC-C,CfPj PIC-PePsPj PrPs 18 CḡPsPeC-PI Cf PIPēPiP°PrPeCf
P·P°CfC,PsCfCfPIP°PSPSCl P·P° C-PSCēPēPjPē PiPsPeP°P·P°PSPSClPjPē (PSP°PiCḡPēPeP»P°Pr,
Cf CḡP°P·C- PIPēCḡP°P·PePsPIPsPiPs PePsP»C-C,Cf) PSPμ PsC†C-PSCḡPIP°P»PēCfCf. P''P°PSC-
PIC-PrCfCfC,PSC-.

PŸPiPsCfC-P± P·P°CfC,PsCfCfPIP°PSPSCl

P''P»Cf PiPμCḡPsCḡP°P»CHPSPsPiPs P·P°CfC,PsCfCfPIP°PSPSCl.

PŸPsC,,P°C†PēC,PēPSC-P± P·P°CfC,PsCfCfPICfCḡC,CH PiPμCḡPsCḡP°P»CHPSPs PiC-Pr C†P°Cf
C—PrPē P°P±Ps PSPμP·P°P»PμP¶PSPs PIC-Pr PiCḡPēPNēPsPjCf C—P¶C-.

P''P»Cf PiP°C†C-C''PSC,C-PI C-P· CfCfPeP»P°PrPSPμPSPēPj PePsPIC,P°PSPSClPj
C,P°P±P»PμC,PePē C,PsC,,P°C†PēC,PēPSC-P±Cf PjPsP¶PSP° PiPsPrCḡC-P±PSPēC,Pē PNē
PrP°C,Pē PiCḡPsPePsPIC,PSCfC,Pē P· PIPsPrPsCḡ.

P''C-C,Pē.

P—P°CfC,PsCfCfPIP°PSPSCl PiCḡPμPiP°CḡP°C,Cf PḡCfPμP»CHCfPSP· Cf C,,PsCḡPjC-
C,P°P±P»PμC,PsPe Cf PrPsP·CfPIP°PSPSC- 5 PjPi, PrP»Cf P»C-PeCfPIP°PSPSCl
P°PeC,PēPIPSPsPiPs PiPsP»C-P°CḡC,PēPeCfP»CfCḡPSPsPiPs CḡPIPμPSC-P»CHPSPsPiPs
C-PrC-PsPiP°C,PēC†PSPsPiPs P°CḡC,CḡPēC,Cf (PiPsP»C-P°CḡC,CḡPēC,Cf P·
PiPsP·PēC,PēPIPSPēPj [RF] P°P±Ps PSPμPiP°C,PēPIPSPēPj [RF-] CḡPμP·CfP»CHC,P°C,PsPj
C,PμCfC,Cf PSP° CḡPμPIPjP°C,PsC—PrPSPēPNē C,,P°PeC,PsCḡ C- PiPsCēPēCḡPμPSPsPiPs
PsP»C-PiPsP°CḡC,CḡPēC,Cf) PjPsP¶P»PēPIPμ P»PēCēPμ PrP»Cf PiP°C†C-C''PSC,C-PI
PrPēC,CfC†PsPiPs PIC-PeCf P· PjP°CfPsCḡ C,C-P»P° ≥ 40 PePi.

P'PμP·PiPμPeP° C,P° PμC,,PμPeC,PēPIPSC-CfC,CH P·P°CfC,PsCfCfPIP°PSPSCl
P»C-PeP°CḡCfCHPePsPiPs P·P°CfPsP±Cf PiP°C†C-C''PSC,P°Pj PrPēC,CfC†PsPiPs PIC-PeCf P·P°
C-PSCēPēPjPē PiPsPeP°P·P°PSPSClPjPē, PeCḡC-Pj P°PeC,PēPIPSPsPiPs
PiPsP»C-P°CḡC,PēPeCfP»CfCḡPSPsPiPs CḡPIPμPSC-P»CHPSPsPiPs
C-PrC-PsPiP°C,PēC†PSPsPiPs P°CḡC,CḡPēC,Cf (PiPsP»C-P°CḡC,CḡPēC,Cf P·
PiPsP·PēC,PēPIPSPēPj [RF] P°P±Ps PSPμPiP°C,PēPIPSPēPj [RF-] CḡPμP·CfP»CHC,P°C,PsPj
C,PμCfC,Cf PSP° CḡPμPIPjP°C,PsC—PrPSPēPNē C,,P°PeC,PsCḡ C- PiPsCēPēCḡPμPSPsPiPs
PsP»C-PiPsP°CḡC,CḡPēC,Cf), PSPμ PICfC,P°PSPsPIP»PμPSC-.

PμPμCḡPμPrPsP·CžPIP°PSPSCl.

Pj CḡP°P·C- PiPμCḡPμPrPsP·CfPIP°PSPSCl CḡPμPePsPjPμPSPrCfC''C,CHCfCf
PIC-PrCfC,PμP¶CfPIP°C,Pē PI PiP°C†C-C''PSC,P° PsP·PSP°PePē PNē CfPēPjPiC,PsPjPē
PiPsP±C-C†PSPēC... CḡPμP°PeC†C-PNē. PŸPiPμC†PēC,,C-C†PSPsPiPs P°PSC,PēPrPsC,P° PSP°
PIPēPiP°PrPsPe PiPμCḡPμPrPsP·CfPIP°PSPSCl C,PsC,,P°C†PēC,PēPSC-P±Cf PSPμ C-CfPSCfC''.
PμPsPeP°P·P°PSPμ CfPēPjPiC,PsPjP°C,PēC†PSPμ PNē PiC-PrC,CḡPēPjCfPIP°P»CHPSPμ
P»C-PeCfPIP°PSPSCl.

P''P°PSC- C,,P°CḡPjP°PePsPeC-PSPμC,PēPePē PiC-Pr C†P°Cf PsPrPSPsPeCḡP°C,PSPsPiPs

P·P°CfC,PsCfCfPIP°PSPSCЦ PrPsP· PrPs 100 PjPi PIPeP»CfCfPSPs Cr P·PrPsCfPsPIPëC...
PrPsP±CfPsPIPsP»CHCfC-PI PIPeP°P·CfCfC,CH PSP° C,Pμ, C%Ps CfP»C-Pr
PsCfC-PeCfPIP°C,Pë, C%Ps PìPsPSP°Pr 95 % PIPiPμPrPμPSPsC— PrPsP·Pë P±CfPrPμ
PIPëPIPμPrPμPSPs PìCfPsC,ЦIPIPsPj 24 PìPsPrPëPS.

PμPsP±C-CfPSC- CfPμP°PeCfC-C—.

P PμP·CfPjPμ PìCfPsC,,C-P»Cf P±PμP·PìPμPePë

P PμPIPjP°C,PsC—PrPSPëPNë P°CfC,CfPëC.

PkP°PNëCfP°CfC,C-CëPëPjPë CfPμCfPNëPsP·PSPëPjPë PìPsP±C-CfPSPëPjPë
CfPμP°PeCfC-CIPIjPë P±CfP»Pë CfPμCfPNëPsP·PSC- C-PSC,,PμPeCfC-C— (PrPëPI.
CfPsP·PrC-P» B«PhCfPsP±P»PëPIPsCfC,C- P·P°CfC,PsCfCfPIP°PSPSCЦB»).

Pj PrPsCfP»C-PrP¶PμPSPSC- PrPsPIPiPsCfC,CfPsPePsPIPsC— P±PμP·PìPμPePë Cr PICfC-C”C—
PìPsPìCfP»CfCfC-C— PìP°CfC-C”PSC,C-PI, CIPIPePëPj PìPsPeP°P·P°PSPëPNë C†PμPNë
PìCfPμPìP°CfP°C,, PSP°PNëCfP°CfC,C-CëPëPjPë CfPμCfPNëPsP·PSPëPjPë
C-PSC,,PμPeCfC-CIPIjPë, PìCfPs CIPIeC- PìPsPIC-PrPsPjP»CfP»PsCfCfC PìC-Pr C†P°Cf
P·P°CfC,PsCfCfPIP°PSPSCЦ C,PsC,,P°C†PëC,PëPSC-P±Cf, P±CfP»Pë PìPSPμPIPIPsPSC-Cf
(1,7 %), PsPìPμCfC-P·CfCfCfPëPNë PìPμCfPìPμCf (0,6 %), C-PSC,,PμPeCfC-C—
CfPμCfPsPIPëPIC-PrPSPëC... CëP»CfC...C-PI (0,4 %), C,,P»PμPiPjPsPSP° (0,4 %),
PrPëPIPμCfC,PëPeCfP»C-C, (0,3 %) C,P° P°PìPμPSPPrPëC†PëC, (0,2 %). PÿPμCfPμPr
PsPìPsCfC,CfPSC-CfBC,PëCfPSPëC... C-PSC,,PμPeCfC-PNë, P·P°CfPμC”CfC,CfPsPIP°PSPëC...
PìC-Pr C†P°Cf P·P°CfC,PsCfCfPIP°PSPSCЦ C,PsC,,P°C†PëC,PëPSC-P±Cf, P±CfP»Pë
C,CfP±PμCfPeCfP»CHPsP· C,P° C-PSC€C- PjC-PePsP±P°PeC,PμCfC-P°P»CHPSC-
C-PSC,,PμPeCfC-C—, PeCfPëPìC,PsPePsPePsP·, PìC-CfC,PsPìP»P°P·PjPsP·, PeP°PSPPrPëPrPsP·
CfC,CfP°PIPsC...PsPrCf, PjCfP»CHC,PëPrPμCfPjP°C,PsPjPSPëPNë PsPìPμCfC-P·CfCfCfPëPNë
PìPμCfPìPμCf, C†PëC,PsPjPμPìP°P»PsPIC-CfCfCfPSC- C-PSC,,PμPeCfC-C—, BK-
PIC-CfCfCfPSC- C-PSC,,PμPeCfC-C— C,P° P»C-CfC,PμCfC-PsP·. P”PμCIPIeC-
PìP°CfC-C”PSC,Pë PjP°P»Pë PrPëCfPμPjC-PSPsPIP°PSC-, P° PSPμ P»PsPeP°P»C-P·PsPIP°PSC-
C,,PsCfPjPë P·P°C...PIPsCfCfPIP°PSPSCЦ. PÿP°PePsP¶ PjPsP¶CfC,CH PIPëPSPëPeP°C,Pë
C-PSC€C- CfPμCfPNëPsP·PSC- C-PSC,,PμPeCfC-C—, PìCfPs CIPIeC- PSPμ
PìPsPIC-PrPsPjP»CfP»PsCfCfC PI PeP»C-PSC-CfPSPëC... PrPsCfP»C-PrP¶PμPSPSCЦC...
(PSP°PìCfPëPeP»P°Pr, PePsPeC†PëPrC-PsC—PrPsPjC-PePsP·).

PkP°PNëCfP°CfC,C-CëPëPjPë PìPsP±C-CfPSPëPjPë CfPμP°PeCfC-CIPIjPë, PìCfPs CIPIeC-
PìPsPIC-PrPsPjP»CfP»PsCfCfC PìCfPsC,CIPIPiPsPj PìPμCfCëPëC... 3 PjC-CfCfCfC-PI
C,PμCfP°PìC-C— PI PìPsPrPIC-PNëPSPëC... CfP»C-PìPëC... PrPsCfP»C-PrP¶PμPSPSCЦC...,
PePsPSC,CfPsP»CHPsPIP°PSPëC... P·P° PrPsPìPsPjPsPìPsCf PìP»P°C†PμP±Ps P°P±Ps
PjPμC,PsC,CfPμPeCfP°C,Cf, P±CfP»Pë PìPsP»PsPIPSPëPNë P±C-P»CH (3,9 %),
C-PSC,,PμPeCfC-C— PIPμCfC...PSC-C... PrPëC...P°P»CHPSPëC... CëP»CfC...C-PI (3,8 %),
PIC-CfCfCfPSP° C-PSC,,PμPeCfC-Cf PIPμCfC...PSC-C... PrPëC...P°P»CHPSPëC...
CëP»CfC...C-PI (3,3 %), PrC-P°CfPμCf (2,9 %), PSCfPrPsC,P° (2,7 %) C,P°
P°CfC,PμCfC-P°P»CHPSP° PìC-PìPμCfC,PμPSP·C-Cf (2,2 %).

PSP°CfC,PeP° PìP°C†C-C”PSC,C-PI, CIPIPePëPj P±CfP»Ps PìCfPëPìPëPSPμPSPs C,PμCfP°PìC-Cf
C†PμCfPμP· PìPsP±C-CfPSC- CfPμP°PeCfC-C— PìCfPsC,CIPIPiPsPj PìPμCfCëPëC...
3 PjC-CfCfCfC-PI C,PμCfP°PìC-C— PI PìPsPrPIC-PNëPSPëC... CfP»C-PìPëC...
PrPsCfP»C-PrP¶PμPSPSCЦC..., PePsPSC,CfPsP»CHPsPIP°PSPëC... P·P° PrPsPìPsPjPsPìPsCf
PìP»P°C†PμP±Ps P°P±Ps PjPμC,PsC,CfPμPeCfP°C,Cf, CfC,P°PSPsPIPëP»P° 3,8 % CfPμCfPμPr

РiР°C†C-C"PSC,C-PI, CИРeC- PsC,CHPëPjCfPIP°P»Pë C,PsC,,P°C†PëC,PëPSC-P±.
PкP°PNëC†P°C†C,C-CëPëPjPë C-PSC,,PµPec†C-CИPjPë, CИРeC- PïCHPëP·PIPsPrPëP»Pë PrPs
PïCHPëPïPëPSPµPSPSCИ C,PµCHP°PïC-C— PïCHPSc,CИPiPsPj PïPµCHCëPëC...
3 PjC-C†CИC†C-PI, C† PePsPSC,CHPsP»CHPsPIP°PSPëC... PeP»C-PSC-C†PSPëC...
PrPsC†P»C-PrP¶PµPSPSCИC..., P±C†P»Pë PsPïPµCHC-P·C†CHC†PëPNë PiPµCHPïPµC† (0,19 %) C-
PïPSPµPIPjPsPSC-CИ (0,15 %).

PµC†PsCHC-P°C,PëC†PSPëPNë P°CHC,CHPëC,

P—P°PiP°P»PsPj PïCHPSc,,C-P»CH P±PµP·PïPµPePë, C%Ps C†PïPsC†C,PµCHC-PiP°PIC†CИ PI
PïP°C†C-C"PSC,C-PI P· P°PeC,PëPIPSPëPj PµC†Pë, CИРeC- PsC,CHPëPjCfPIP°P»Pë
C,PsC,,P°C†PëC,PëPSC-P±, C†P·PiPsPrP¶C†PIP°PIC†CИ P· PïCHPSc,,C-P»PµPj P±PµP·PïPµPePë,
C%Ps C†PïPsC†C,PµCHC-PiP°PIC†CИ PI PïP°C†C-C"PSC,C-PI C-P· P Pë, CИРeC-
PsC,CHPëPjCfPIP°P»Pë C,PsC,,P°C†PëC,PëPSC-P±.

PëPSPeC-P»PsP·C†CHC†PëPNë C†PïPsPSPrPëP»C-C,

P—P°PiP°P»PsPj PïCHPSc,,C-P»CH P±PµP·PïPµPePë, C%Ps C†PïPsC†C,PµCHC-PiP°PIC†CИ PI
PïP°C†C-C"PSC,C-PI P· P°PeC,PëPIPSPëPj B PëPë, CИРeC- PsC,CHPëPjCfPIP°P»Pë
C,PsC,,P°C†PëC,PëPSC-P±, C†P·PiPsPrP¶C†PIP°PIC†CИ P· PïCHPSc,,C-P»PµPj P±PµP·PïPµPePë,
C%Ps C†PïPsC†C,PµCHC-PiP°PIC†CИ PI PïP°C†C-C"PSC,C-PI C-P· P Pë, CИРeC-
PsC,CHPëPjCfPIP°P»Pë C,PsC,,P°C†PëC,PëPSC-P±.

P'PëCHP°P·PePsPIPëPNë PePsP»C-C,

PкP°PNëC†P°C†C,C-CëPµ PïPsPIC-PrPsPjP»CИP»PsC†CИ PïCHPs PïPsP±C-C†PSC-
CHPµP°PeC†C-C— PI PïP°C†C-C"PSC,C-PI, CИРeC- PsC,CHPëPjCfPIP°P»Pë
C,PsC,,P°C†PëC,PëPSC-P± C† PrPsP·C- 10 PjPi PrPIP° CHP°P·Pë PSP° PrPsP±C† PïC-Pr C†P°C†
PrPsC†P»C-PrP¶PµPSCH C-PSPrC†PeC†C-PNëPSPSc— C,PµCHP°PïC-C—; C†Pµ P±C†P»Pë
PiPsP»PsPIPSPëPNë P±C-P»CH, PSP°P·PsC,,P°CHPëPSPiC-C,, PSC†PrPsC,P° PNë
P°CHC,CHP°P»PiC-CИ.

Pj PrPsC†P»C-PrP¶PµPSPSCИC... C-PSPrC†PeC†C-PNëPSPSc— C,P°
PïC-PrC,CHPëPjCfPIP°P»CHPsPSc— C,PµCHP°PïC-C— PI PïCHC†PïP°C... P»C-PeC†PIP°PSPSCИ
C,PsC,,P°C†PëC,PëPSC-P±PsPj C- PïP»P°C†PµP±Ps PSP°PNëC†P°C†C,C-CëPëPjPë
PeP°C,PµPiPsCHC-CИPjPë C†PµCHPNëPsP·PSPëC... PïPsP±C-C†PSPëC... CHPµP°PeC†C-PNë
P±C†P»Pë CHPsP·P»P°PrPë P· P±PsPeC† CëP»C†PSPePsPIPs-PePëCëPePsPIPsPiPs C,CHP°PeC,C†
PNë C-PSC,,PµPeC†C-C—, P° PSP°PNëC†P°C†C,C-CëPsCH C†PµCHPNëPsP·PSPScH
PïPsP±C-C†PSPScH CHPµP°PeC†C-C"CH P±C†P»Ps PïPsPiC-CHCëPµPSPSCИ PïPµCHPµP±C-PiC†
P'Pë.

P—P°PiP°P»PsPj PïCHPSc,,C-P»CH P±PµP·PïPµPePë, C%Ps C†PïPsC†C,PµCHC-PiP°PIC†CИ PI
PïP°C†C-C"PSC,C-PI C-P· P'Pë, CИРeC- PsC,CHPëPjCfPIP°P»Pë C,PsC,,P°C†PëC,PëPSC-P±,
C†P·PiPsPrP¶C†PIP°PIC†CИ P· PïCHPSc,,C-P»PµPj P±PµP·PïPµPePë C,PsC,,P°C†PëC,PëPSC-P±C†
PI CHP°P·C- P·P°C†C,PsC†C†PIP°PSPSCИ P·P° PïPsPeP°P·P°PSPSCИPj P Pë.

PëPïPëC†PsPe PïPsP±C-C†PSPëC... CHPµP°PeC†C-PNë

PµPsP±C-C†PSC- CHPµP°PeC†C-C—, PïPµCHPµP»C-C†PµPSC- PSPëP¶C†Pµ, P±C†P»Pë
P·P°CHPµC"†C,CHPsPIP°PSC- PI PeP»C-PSC-C†PSPëC... PrPsC†P»C-PrP¶PµPSPSCИC...
C† PïP°C†C-C"PSC,C-PI C-P· P Pë, PµC†Pë, PëPë C- P'Pë. P PµP°PeC†C-C—
PeP»P°C†PëC,,C-PePsPIP°PSC- P·P° C†PëC†C,PµPjPSPs-PsCHPïP°PSPSPëPjPë PeP»P°C†P°PjPë
C- C,P°PePëPjPë P·P°PiP°P»CHPsPïCHPëPNëPSCИC,PëPjPë PeP°C,PµPiPsCHC-CИPjPë

C $\ddot{P}^{\circ}$ C $\dot{I}$ C,PsC,P $\ddot{e}$ PIP $\ddot{e}$ PSP $\ddot{e}$ PePSP μ PSPSC $\dot{I}$: PrC $\acute{r}$ P $\dot{I}$ μ C $\ddot{P}^{\circ}$ C $\dot{I}$ C,Ps ($\geq 1/10$), C $\ddot{P}^{\circ}$ C $\dot{I}$ C,Ps (PIC-Pr $\geq 1/100$ PrPs $< 1/10$), PSP μ C $\ddot{P}^{\circ}$ C $\dot{I}$ C,Ps (PIC-Pr $\geq 1/1000$ PrPs $< 1/100$), C $\dot{H}$ C-PrPePs (PIC-Pr $\geq 1/10\ 000$ PrPs $< 1/1000$), PrC $\acute{r}$ P $\dot{I}$ μ C $\dot{H}$ C-PrPePs ($< 1/10\ 000$) P $^{\circ}$ P $\pm$ Ps C $\ddot{P}^{\circ}$ C $\dot{I}$ C,PsC,P $^{\circ}$ PSP μ PIC-PrPsPjP $^{\circ}$ (PSP μ PjPsP $\dot{I}$ PSP $^{\circ}$ PsC $\dot{I}$ C-PSP $\ddot{e}$ C,P $\ddot{e}$ P $\cdot$ P $^{\circ}$ PSP $^{\circ}$ C $\dot{I}$ PIPS $\ddot{e}$ PjP $\ddot{e}$ PrP $^{\circ}$ PSP $\ddot{e}$ PjP $\ddot{e}$). Pj PePsP $\dot{I}$ PSC-PN $\ddot{e}$ PiC $\dot{H}$ C $\acute{r}$ PiC- C $\ddot{P}^{\circ}$ C $\dot{I}$ C,PsC,P $\ddot{e}$ PiPsP $\pm$ C-C $\ddot{P}$ SC- C $\dot{H}$ P μ P $^{\circ}$ PeC $\dot{I}$ C-C- P $\ddot{I}$ μ C $\dot{H}$ P μ P $\gg$ C-C $\ddot{P}$ μ PSC- PI PiPsC $\dot{H}$ C $\dot{I}$ PrPeC $\acute{r}$ P $\cdot$ PSP $\ddot{e}$ P $\dot{I}$ μ PSPSC $\dot{I}$ C-C...PSC $\dot{H}$ PsC- C $\dot{I}$ P μ C $\dot{H}$ PN $\ddot{e}$ PsP $\cdot$ PSPsC $\dot{I}$ C,C-.

P $\dot{I}$ PSC,,P μ PeC $\dot{I}$ C-PN $\ddot{e}$ PSC- C,P $^{\circ}$ PiP $^{\circ}$ C $\dot{H}$ P $^{\circ}$ P $\cdot$ P $\ddot{e}$ C,P $^{\circ}$ C $\dot{H}$ PSC- P $\cdot$ P $^{\circ}$ C...PIP s C $\dot{H}$ C $\dot{H}$ PIP $^{\circ}$ PSPSC $\dot{I}$: C $\ddot{P}^{\circ}$ C $\dot{I}$ C,Ps: PiPSP μ PIPjPsPSC-C $\dot{I}$, PiC $\dot{H}$ P $\ddot{e}$ Pi, PsPiP μ C $\dot{H}$ C-P $\cdot$ C $\acute{r}$ C $\dot{H}$ C $\ddot{P}$ PN $\ddot{e}$ PiP μ C $\dot{H}$ PiP μ C $\dot{I}$, C-PSC,,P μ PeC $\dot{I}$ C-C- C $\dot{I}$ P μ C $\ddot{P}$ PsPIP $\ddot{e}$ PIC-PrPSP $\ddot{e}$ C... C $\ddot{e}$ P $\gg$ C $\dot{I}$ C...C-PI, C $\dot{I}$ P $\ddot{e}$ PSC $\acute{r}$ C $\dot{I}$ P $\ddot{e}$ C,, P $\pm$ C $\dot{H}$ PsPSC...C-C,, PSP $^{\circ}$ P $\cdot$ PsC,,P $^{\circ}$ C $\dot{H}$ P $\ddot{e}$ PSPiC-C,, C,,P $^{\circ}$ C $\dot{H}$ P $\ddot{e}$ PSPiC-C,,; PSP μ C $\ddot{P}^{\circ}$ C $\dot{I}$ C,Ps: C,C $\acute{r}$ P $\pm$ P μ C $\dot{H}$ PeC $\acute{r}$ P $\gg$ C $\dot{H}$ PsP $\cdot$, PrP $\ddot{e}$ PIP μ C $\dot{H}$ C,P $\ddot{e}$ PeC $\acute{r}$ P $\gg$ C-C,, PiC-C $^{\circ}$ P $\gg$ PsPSP μ C,,C $\dot{H}$ P $\ddot{e}$ C,, C,,P $\gg$ P μ PiPjPsPSP $^{\circ}$, PiC $\dot{H}$ PsC $\dot{I}$ C,P $\ddot{e}$ PN $\ddot{e}$ PiP μ C $\dot{H}$ PiP μ C $\dot{I}$, PIC-C $\dot{H}$ C $\acute{r}$ C $\dot{I}$ PSP $\ddot{e}$ PN $\ddot{e}$ PiP $^{\circ}$ C $\dot{I}$ C,C $\dot{H}$ PsP μ PSC,P μ C $\dot{H}$ P $\ddot{e}$ C,, PIC-C $\dot{H}$ C $\acute{r}$ C $\dot{I}$ PSP $^{\circ}$ C-PSC,,P μ PeC $\dot{I}$ C-C $\dot{I}$; C $\dot{H}$ C-PrPePs: C $\dot{I}$ P μ PiC $\dot{I}$ P $\ddot{e}$ C $\dot{I}$, C $\acute{r}$ C $\dot{H}$ PsC $\dot{I}$ P μ PiC $\dot{I}$ P $\ddot{e}$ C $\dot{I}$, PrP $\ddot{e}$ C $\dot{I}$ P μ PjC-PSPsPIP $^{\circ}$ PSP $\ddot{e}$ PN $\ddot{e}$ C,C $\acute{r}$ P $\pm$ P μ C $\dot{H}$ PeC $\acute{r}$ P $\gg$ C $\dot{H}$ PsP $\cdot$, P $\pm$ P $^{\circ}$ PeC,P μ C $\dot{H}$ C-C $^{\circ}$ PjC-C $\dot{I}$, PiPSP μ PIPjPsPSC-C $\dot{I}$, C $\dot{I}$ PiC $\dot{H}$ P $\ddot{e}$ C $\ddot{P}$ PSP μ PSP $^{\circ}$ *Pneumocystis jirovecii*, PiPSP μ PIPjPsPSC-C $\dot{I}$ PiPSP μ PIPjPsPePsPePsPIP $^{\circ}$, PiPSP μ PIPjPsPSC-C $\dot{I}$ P $\pm$ P $^{\circ}$ PeC,P μ C $\dot{H}$ C-P $^{\circ}$ P $\gg$ C $\dot{H}$ PSP $^{\circ}$, C $\dot{I}$ P $\ddot{e}$ C,PsPjP μ PiP $^{\circ}$ P $\gg$ PsPIC-C $\dot{H}$ C $\acute{r}$ C $\dot{I}$ PSP $^{\circ}$ C-PSC,,P μ PeC $\dot{I}$ C-C $\dot{I}$, P $^{\circ}$ C $\dot{H}$ C,C $\dot{H}$ P $\ddot{e}$ C, P $\pm$ P $^{\circ}$ PeC,P μ C $\dot{H}$ C-P $^{\circ}$ P $\gg$ C $\dot{H}$ PSP $\ddot{e}$ PN $\ddot{e}$; PrC $\acute{r}$ P $\dot{I}$ μ C $\dot{H}$ C-PrPePs: C,C $\acute{r}$ P $\pm$ P μ C $\dot{H}$ PeC $\acute{r}$ P $\gg$ C $\dot{H}$ PsP $\cdot$ C $\dot{I}$ P μ PSC,C $\dot{H}$ P $^{\circ}$ P $\gg$ C $\dot{H}$ PSPsC- PSP μ C $\dot{H}$ PIPsPIPsC- C $\dot{I}$ P $\ddot{e}$ C $\dot{I}$ C,P μ PjP $\ddot{e}$, PjP μ PSC-PSPiC-C, PeC $\dot{H}$ P $\ddot{e}$ PiC,PsPePsPePsPIP $\ddot{e}$ PN $\ddot{e}$, PSP μ PeC $\dot{H}$ PsC,P $\ddot{e}$ P $\cdot$ C $\acute{r}$ C $\dot{H}$ C $\ddot{P}$ PN $\ddot{e}$ C,,P $^{\circ}$ C $\dot{I}$ C $\dot{I}$ P $\ddot{e}$ C-C,, P μ PSC $\dot{I}$ P μ C,,P $^{\circ}$ P $\gg$ C-C,, C $\dot{I}$ C,P $^{\circ}$ C,,C-P $\gg$ PsPePsPePsPIP $^{\circ}$ P $\pm$ P $^{\circ}$ PeC,P μ C $\dot{H}$ C-C $^{\circ}$ PjC-C $\dot{I}$, C-PSC,,P μ PeC $\dot{I}$ C-C $\dot{I}$, C $\dot{I}$ PiC $\dot{H}$ P $\ddot{e}$ C $\ddot{P}$ PSP μ PSP $^{\circ}$ PePsPjPiP $\gg$ P μ PeC $\dot{I}$ PsPj *Mycobacterium avium*, P $^{\circ}$ C,P $\ddot{e}$ PiPsPIP $^{\circ}$ PjC-PePsP $\pm$ P $^{\circ}$ PeC,P μ C $\dot{H}$ C-P $^{\circ}$ P $\gg$ C $\dot{H}$ PSP $^{\circ}$ C-PSC,,P μ PeC $\dot{I}$ C-C $\dot{I}$.

P $^{\circ}$ PsP $\pm$ C $\dot{H}$ PsC $\dot{I}$ PeC-C $\dot{I}$ PSC-, P $\cdot$ P $\gg$ PsC $\dot{I}$ PeC-C $\dot{I}$ PSC- C,P $^{\circ}$ PSP μ C $\acute{z}$ C,PsC $\ddot{P}$ PSP μ PSC- PSPsPIP s C $\acute{z}$ C,PIPsC $\dot{H}$ P μ PSPSC $\dot{I}$ (PIPeP $\gg$ C $\dot{H}$ C $\ddot{P}$ PSPs P $\cdot$ PeC-C $\dot{I}$ C,P $^{\circ}$ PjP $\ddot{e}$ PN $\ddot{e}$ PiPsP $\gg$ C-PiP $^{\circ}$ PjP $\ddot{e}$): PSP μ C $\ddot{P}^{\circ}$ C $\dot{I}$ C,Ps: C $\dot{H}$ P $^{\circ}$ Pe P $\gg$ P μ PiP μ PSCH $\dot{H}$, PSP μ PjP μ P $\gg$ P $^{\circ}$ PSPsPjPSP $\ddot{e}$ PN $\ddot{e}$ C $\dot{H}$ P $^{\circ}$ Pe C $\ddot{e}$ PeC-C $\dot{H}$ P $\ddot{e}$; C $\dot{H}$ C-PrPePs: P $\gg$ C-PjC,,PsPjP $^{\circ}$.

P PsP $\cdot$ P $\gg$ P $^{\circ}$ PrP $\ddot{e}$ P $\cdot$ P $\pm$ PsPeC $\acute{z}$ PeC $\dot{H}$ PsPIPsPSPsC $\dot{I}$ PSPsC- C,P $^{\circ}$ P $\gg$ C-PjC,,P $^{\circ}$ C,P $\ddot{e}$ C $\ddot{P}$ PSPsC- C $\dot{I}$ P $\ddot{e}$ C $\dot{I}$ C,P μ Pj: C $\ddot{P}^{\circ}$ C $\dot{I}$ C,Ps: P $\gg$ C-PjC,,PsPiP μ PSC-C $\dot{I}$, P $^{\circ}$ PSP μ PjC-C $\dot{I}$; PSP μ C $\ddot{P}^{\circ}$ C $\dot{I}$ C,Ps: P $\gg$ P μ PN $\ddot{e}$ PePsPiP μ PSC-C $\dot{I}$, PSP μ PN $\ddot{e}$ C,C $\dot{H}$ PsPiP μ PSC-C $\dot{I}$.

P PsP $\cdot$ P $\gg$ P $^{\circ}$ PrP $\ddot{e}$ P $\cdot$ P $\pm$ PsPeC $\acute{z}$ C-PjC $\acute{z}$ PSPSPsC- C $\dot{I}$ P $\ddot{e}$ C $\dot{I}$ C,P μ PjP $\ddot{e}$: C $\ddot{P}^{\circ}$ C $\dot{I}$ C,PsC,P $^{\circ}$ PSP μ PIC-PrPsPjP $^{\circ}$: PiC-PiP μ C $\dot{H}$ C $\ddot{P}$ C $\acute{r}$ C,P $\gg$ P $\ddot{e}$ PIC-C $\dot{I}$ C,C $\dot{H}$ *, P $^{\circ}$ PSPiC-PsPSP μ PIC $\dot{H}$ PsC,P $\ddot{e}$ C $\ddot{P}$ PSP $\ddot{e}$ PN $\ddot{e}$ PSP $^{\circ}$ P $\pm$ C $\dot{H}$ C $\dot{I}$ Pe*, PeC $\dot{H}$ PsPiP $\ddot{e}$ PIB $\dot{H}$ ™ C $\dot{I}$ IPSP $\ddot{e}$ P $^{\circ}$ *.

P PsP $\cdot$ P $\gg$ P $^{\circ}$ PrP $\ddot{e}$ C...P $^{\circ}$ C $\dot{H}$ C $\ddot{P}$ C $\acute{z}$ PIP $^{\circ}$ PSPSC $\dot{I}$ C,P $^{\circ}$ PiPsC $\dot{H}$ C $\acute{z}$ C $\ddot{e}$ P μ PSPSC $\dot{I}$ PsP $\pm$ PjC-PSC $\acute{z}$ C $\dot{H}$ P μ C $\ddot{P}$ PsPIP $\ddot{e}$ PS: PSP μ C $\ddot{P}^{\circ}$ C $\dot{I}$ C,Ps: PrP $\ddot{e}$ C $\dot{I}$ P $\gg$ C-PiC-PrP μ PjC-C $\dot{I}$, PiC-PiP μ C $\dot{H}$ P $\gg$ C-PiC-PrP μ PjC-C $\dot{I}$, P $\cdot$ PSP μ PIPsPrPSP μ PSPSC $\dot{I}$.

P μ C $\dot{I}$ P $\ddot{e}$ C...C-C $\ddot{P}$ SC- C $\dot{H}$ PsP $\cdot$ P $\gg$ P $^{\circ}$ PrP $\ddot{e}$: PSP μ C $\ddot{P}^{\circ}$ C $\dot{I}$ C,Ps: P $\pm$ P μ P $\cdot$ C $\dot{I}$ PsPSPSC $\dot{I}$.

P PsP $\cdot$ P $\gg$ P $^{\circ}$ PrP $\ddot{e}$ P $\cdot$ P $\pm$ PsPeC $\acute{z}$ PSP μ C $\dot{H}$ PIPsPIPsC- C $\dot{I}$ P $\ddot{e}$ C $\dot{I}$ C,P μ PjP $\ddot{e}$: C $\ddot{P}^{\circ}$ C $\dot{I}$ C,Ps: PiPsP $\gg$ PsPIPS $\ddot{e}$ PN $\ddot{e}$ P $\pm$ C-P $\gg$ C $\dot{H}$; PSP μ C $\ddot{P}^{\circ}$ C $\dot{I}$ C,Ps: PiP $^{\circ}$ C $\dot{H}$ P μ C $\dot{I}$ C,P μ P $\cdot$ C-C $\dot{I}$.

P PsP $\cdot$ P $\gg$ P $^{\circ}$ PrP $\ddot{e}$ P $\cdot$ P $\pm$ PsPeC $\acute{z}$ C $\dot{I}$ P μ C $\dot{H}$ C $\dot{I}$ C $\dot{I}$: PSP μ C $\ddot{P}^{\circ}$ C $\dot{I}$ C,Ps: C-PSC,,P $^{\circ}$ C $\dot{H}$ PeC,

PjC-PsPeP°CḡPrP°.

PŸCžPrPëPSPSC- CḡPsP·P»P°PrPë: C‡P°CḡC,Ps: P°CḡC,PμCḡC-P°P»CHbPSP°
PiC-PiPμCḡC,PμPSP·C-Cḡ; PSPμC‡P°CḡC,Ps: PIPμPSPsP·PSP° C,CḡPsPjP±PsPμPjP±PsP»C-Cḡ**.

P PsP·P»P°PrPë P· P±PsPeCž CḡPëCḡC,PμPjPë PrPëC...P°PSPSCḡ, PsCḡPiP°PSC-PI
PiCḡCžPrPSPsC— PeP»C-C,PePë C,P° CḡPμCḡPμPrPsCḡC,C-PSPSCḡ: C‡P°CḡC,Ps:
PeP°C€PμP»CHb; PSPμC‡P°CḡC,Ps: PrPëCḡPiPSPsPμ, PSP°P±CḡCḡPe PiCḡPëPrP°C,PePsPIPëC...
PiP°P·CḡC... PSPsCḡP°.

P PsP·P»P°PrPë P· P±PsPeCž C€P»CžPSPePsPIPs-PePëC€PePsPIPsPiPs C,CḡP°PeC,Cž: C‡P°CḡC,Ps:
P±C-P»CHb Cḡ PḡPëPIPsC,C-, P±P»CḡPIP°PSPSCḡ, PrC-P°CḡPμCḡ, PSCḡPrPsC,P°,
PiP°CḡC,CḡPëC,, PrPëCḡPiPμPiCḡC-Cḡ.

P PsP·P»P°PrPë P· P±PsPeCž PiPμPiP°C,PsP±C-P»C-P°CḡPSPsC— CḡPëCḡC,PμPjPë:
PSPμC‡P°CḡC,Ps: CḡC,PμP°C,PsP· PiPμC‡C-PSPePë, PiC-PrPIPëC%oPμPSPSCḡ CḡC-PIPS-C-PIB
PiPμC‡C-PSPePsPIPëC... C,,PμCḡPjPμPSC,C-PI, PiC-PrPIPëC%oPμPSPSCḡ CḡC-PIPS-C-PI
C,CḡP°PSCḡP°PjC-PSP°P·, PiC-PrPIPëC%oPμPSPSCḡ CḡC-PIPSḡ PiP°PjPjP°-
PiP»CḡC,P°PjC-P»C,CḡP°PSCḡC,,PμCḡP°P·Pë; CḡC-PrPePs: PIC-PrC...PëP»PμPSPSCḡ PIC-Pr
PSPsCḡPjPë CḡPμP·CḡP»CHbC,P°C,C-PI C,,CḡPSPeC‡C-PsPSP°P»CHbPSPsC— PiCḡPsP±Pë
PiPμC‡C-PSPePë.

P PsP·P»P°PrPë P· P±PsPeCž C€PeC-CḡPë C,P° PiC-PrC€PeC-CḡPSPsC— PeP»C-C,PePsPIPëPSPë:
C‡P°CḡC,Ps: PIPëCḡPëPi, P°PePSPμ; PSPμC‡P°CḡC,Ps: PμCḡPëC,PμPjP°, CḡPIPμCḡP±C-Pḡ.

P PsP·P»P°PrPë P· P±PsPeCž PsPiPsCḡPSPs-CḡCžC...PsPIPsPiPs P°PiP°CḡP°C,Cž C,P°
CḡPiPsP»CžC‡PSPsC— C,PeP°PSPëPSPë: C‡P°CḡC,Ps: P°CḡC,CḡP°P»PiC-Cḡ; PSPμC‡P°CḡC,Ps:
PSP°P±CḡCḡPe CḡCḡPiP»PsP±C-PI, C,PμPSPPrPëPSC-C,; CḡC-PrPePs: Pjḡḡ™CḡP·PsPIPs-
CḡPePμP»PμC,PSPëPNḡ P±C-P»CHb.

P—P°PiP°P»CHbPSC- CḡPsP·P»P°PrPë C,P° CḡPμP°PeC‡C-C— PI PjC-CḡC‡C- PIPIPμPrPμPSPSCḡ:
C‡P°CḡC,Ps: PiPμCḡPëC,,PμCḡPëC‡PSPëPNḡ PSP°P±CḡCḡPe; PSPμC‡P°CḡC,Ps:
P»PëC...PsPjP°PSPeP°, PiC-PrPIPëC%oPμPSP° PIC,PsPjP»CḡPIP°PSC-CḡC,CHb.

PḡP±CḡC,PμPḡPμPSPSCḡ: C‡P°CḡC,Ps: PiC-PrPIPëC%oPμPSPëPNḡ CḡC-PIPμPSCḡ
PeCḡPμP°C,PëPSC,,PsCḡC,,PsPeC-PSP°P·Pë PI PeCḡPsPIC-; PSPμC‡P°CḡC,Ps:
PiC-PrPIPëC%oPμPSPëPNḡ CḡC-PIPμPSCḡ PeCḡPμP°C,PëPSC-PSCḡ PI PeCḡPsPIC-,
PiC-PrPIPëC%oPμPSPSCḡ CḡC-PIPSḡ C...PsP»PμCḡC,PμCḡPëPSCḡ PI PeCḡPsPIC-,
PiC-PrPIPëC%oPμPSPSCḡ CḡC-PIPSḡ C...PsP»PμCḡC,PμCḡPëPSCḡ
P»C-PiPsPiCḡPsC,PμC—PSC-PI PSPëP·CHbPePsC— C%oC-P»CHbPSPsCḡC,C-,
P·P±C-P»CHbC€PμPSPSCḡ PjP°CḡPë C,C-P»P°.

PŸCḡP°PIPjPë, PsC,CḡCžC”PSPSCḡ C,P° CžCḡPeP»P°PrPSPμPSPSCḡ PiCḡPsC‡PμPrCžCḡ:
PSPμC‡P°CḡC,Ps: CḡPsP·C,CḡPiPSPμPSPSCḡ P·Piḡḡ™CḡP·PsPe, CḡPsP·C,CḡPiPSPμPSPSCḡ
Pjḡḡ™CḡP·C-PI.

*B B B P”P°PSC-, PsC,CḡPëPjP°PSC- P·C- CḡPiPsPSC,P°PSPSPëC... PiPsPIC-PrPsPjP»PμPSCḡ.

**B PŸPμCḡPjC-PS B«PIPμPSPsP·PSP° C,CḡPsPjP±PsPμPjP±PsP»C-CḡB» PsC...PsPiP»CḡC”
C,CḡPsPjP±PsPμPjP±PsP»C-Cḡ P»PμPiPμPSPμPIPsC— P°CḡC,PμCḡC-C— (PŸP·P·Ph),
C,CḡPsPjP±PsP· PiP»PëP±PsPePëC... PIPμPS (PŸP”P”) C,P° C,CḡPsPjP±PsP· PIPμPS

P+PSC,,PuPeC+C-C— PI C+C-P»PsPiCr

P PμPIPJ°C,PsC—PrPSPëPNë P°CĤC,CĤPëC,

PJ PePsPSC,CĤPsP»CHbPsPIP°PSPëC... PeP»C-PSC-C†PSPëC... PrPsCĤP»C-PrP¶PμPSPSCĤC...
C,,P°P·Pë 3 C†P°CĤC,PsC,P° PIPëPSPëPePSPμPSPSCĤ C-PSC,,PμPeC†C-PNë PïCĤPsC,CĤPiPsPj
PïPμCĤC-PsPrC† C†PμCĤPμP· 0бĤ“3 PjC-CĤCĤC†C- PïC-CĤP»CĤ PïPsC†P°C,PeC†
C,PμCĤP°PïC-C— C† PïCĤC†PïP°C... PjPsPSPsC,PμCĤP°PïC-C— C,PsC,,P°C†PëC,PëPSC-P±PsPj C†
PrPsP·C- 5 PjPi PrPIP° CĤP°P·Pë PSP° PrPsP±C† (P·P°PiP°P»PsPj 616 PïP°C†C-C”PSC,C-PI) C-
10 PjPi PrPIP° CĤP°P·Pë PSP° PrPsP±C† (P·P°PiP°P»PsPj 642 PïP°C†C-C”PSC,Pë)
CĤC,P°PSPsPIPëP»P° 16,2 % (100 PïP°C†C-C”PSC,C-PI) C,P° 17,9 % (115 PïP°C†C-C”PSC,C-PI)
PIC-PrPïPsPIC-PrPSPs, PïPsCĤC-PIPSCĤPSPs P· 18,9 % (23 PïP°C†C-C”PSC,Pë) C† PïCĤC†PïC-
PïP»P°C†PμP±Ps (P·P°PiP°P»PsPj 122 PïP°C†C-C”PSC,Pë). PJ PePsPSC,CĤPsP»CHbPsPIP°PSPëC...
PeP»C-PSC-C†PSPëC... PrPsCĤP»C-PrP¶PμPSPSCĤC... C,,P°P·Pë 3 C-P·
P·P°CĤC,PsCĤC†PIP°PSPSCĤPj CĤC†PïC†C,PSCHbPsC— C,PμCĤP°PïC-C— DMARD C†P°CĤC,PsC,P°
PIPëPSPëPePSPμPSPSCĤ C-PSC,,PμPeC†C-PNë PïCĤPsC,CĤPiPsPj 0бĤ“3 PjC-CĤCĤC†C-PI
PïC-CĤP»CĤ PïPsC†P°C,PeC† C,PμCĤP°PïC-C— C† PïCĤC†PïC- C,PsC,,P°C†PëC,PëPSC-P±C† PI
PrPsP·C- 5 PjPi PrPIP° CĤP°P·Pë PSP° PrPsP±C† (P·P°PiP°P»PsPj 973 PïP°C†C-C”PSC,Pë)
C- 10 PjPi PrPIP° CĤP°P·Pë PSP° PrPsP±C† (P·P°PiP°P»PsPj 969 PïP°C†C-C”PSC,C-PI) PïP»CĤC†
DMARD CĤC,P°PSPsPIPëP»P° 21,3 % (207 PïP°C†C-C”PSC,C-PI)
C- 21,8 % (211 PïP°C†C-C”PSC,C-PI) PIC-PrPïPsPIC-PrPSPs, PïPsCĤC-PIPSCĤPSPs P· 18,4 %
(103 PïP°C†C-C”PSC,Pë) C† PïCĤC†PïC- PïP»P°C†PμP±Ps PïP»CĤC† DMARD (P·P°PiP°P»PsPj
559 PïP°C†C-C”PSC,C-PI).

Pk°PNëC†P°CĤC,C-CëPëPjPë C-PSC,,PμPeC†C-CĤPjPë P±C†P»Pë C-PSC,,PμPeC†C-C—
PIPμCĤC...PSC-C... PrPëC...P°P»CHbPSPëC... CëP»CĤC...C-PI C- PSP°P·PsC,,P°CĤPëPSPiC-C, (3,7
C- 3,2 % PIC-PrPïPsPIC-PrPSPs).

P—P°PiP°P»CHbPSP° C†P°CĤC,PsC,P° PIPëPSPëPePSPμPSPSCĤ C-PSC,,PμPeC†C-PNë C†
PïPsPïC†P»CĤC†C— PrP»CĤ PsC†C-PSCHbPIP°PSPSCĤ PrPsPIPiPsCĤC,CĤPsPePsPiPsC—
P±PμP·PïPμPePë, PrPs CĤPePsC— PIPeP»CĤC†P°P»Pë PïP°C†C-C”PSC,C-PI, C°°Ps
PsC,CĤPëPjC†PIP°P»Pë C,PsC,,P°C†PëC,PëPSC-P± P·P° PICĤC-PjP° CĤC...PIP°P»PμPSPëPjPë
PïPsPeP°P·P°PSPSCĤPjPë (P·P°PiP°P»PsPj 4867 PïP°C†C-C”PSC,C-PI), CĤC,P°PSPsPIPëP»P°
46,1 PïP°C†C-C”PSC,P° P· PIC-PrPïPsPIC-PrPSPëPjPë PïPsP±C-C†PSPëPjPë CĤPμP°PeC†C-CĤPjPë
PSP° 100 PïP°C†C-C”PSC,Ps-CĤPsPeC-PI (43,8 C- 47,2 PïP°C†C-C”PSC,P° P·
PIC-PrPïPsPIC-PrPSPëPjPë PïPsP±C-C†PSPëPjPë CĤPμP°PeC†C-CĤPjPë PrP»CĤ CĤC...PμPj
PrPsP·C†PIP°PSPSCĤ 5 PjPi C- 10 PjPi PrPIP° CĤP°P·Pë PSP° PrPsP±C† PIC-PrPïPsPIC-PrPSPs).
PJ PïP°C†C-C”PSC,C-PI (P·P°PiP°P»PsPj 1750), CĤPeC- PsC,CĤPëPjC†PIP°P»Pë PïCĤPμPïP°CĤP°C,
C† CĤPePsCĤC,C- PjPsPSPsC,PμCĤP°PïC-C—, PïPsPeP°P·PSPëPePë C†P°CĤC,PsC,Pë
PIPëPSPëPePSPμPSPSCĤ C-PSC,,PμPeC†C-PNë CĤC,P°PSPsPIPëP»Pë 48,9 C-
41,9 PïP°C†C-C”PSC,C-PI P· PIC-PrPïPsPIC-PrPSPëPjPë CĤPμP°PeC†C-CĤPjPë PSP°
100 PïP°C†C-C”PSC,Ps-CĤPsPeC-PI PrP»CĤ CĤC...PμPj PrPsP·C†PIP°PSPSCĤ 5 PjPi C,P° 10 PjPi
PrPIP° CĤP°P·Pë PSP° PrPsP±C† PIC-PrPïPsPIC-PrPSPs. P”P»CĤ PïP°C†C-C”PSC,C-PI
(P·P°PiP°P»PsPj 3117), CĤPeC- PsC,CĤPëPjC†PIP°P»Pë CĤC†PïC†C,PSCH C,PμCĤP°PïC-CĤ
DMARD, PïPsPeP°P·PSPëPePë C†P°CĤC,PsC,Pë PIPëPSPëPePSPμPSPSCĤ C-PSC,,PμPeC†C-PNë
CĤC,P°PSPsPIPëP»Pë 41,0 C- 50,3 PïP°C†C-C”PSC,P° P· PIC-PrPïPsPIC-PrPSPëPjPë
CĤPμP°PeC†C-CĤPjPë PSP° 100 PïP°C†C-C”PSC,Ps-CĤPsPeC-PI PrP»CĤ CĤC...PμPj
PrPsP·C†PIP°PSPSCĤ 5 PjPi C- 10 PjPi PrPIP° CĤP°P·Pë PSP° PrPsP±C† PIC-PrPïPsPIC-PrPSPs.

PĤPSPeC-P»PsP·CžCĤC†PëPNë CĤPïPsPSPrPëP»C-C,

P—PïC-PrPSPs P· PsP±бĤ™ C”PrPSP°PSPëPjPë PrP°PSPëPjPë P· PeP»C-PSC-C†PSPëC...
PrPsCĤP»C-PrP¶PμPSCH C,,P°P·Pë 2 C,P° C,,P°P·Pë 3, PïCĤPsC,CĤPiPsPj PïP»P°C†PμP±Ps-
PePsPSC,CĤPsP»CHbPsPIP°PSPsPiPs PïPμCĤC-PsPrC† C,CĤPëPIP°P»C-CĤC,CĤ PrPs

16 C, PëP¶PSC-PI C†P°CÍC, PsC, P° PIPëPSPëPePSPµPSPSC¶ C-PSC, µPeC†C-PNë Cr PiC¶C†PíC-, C¶PeP° PsC, C¶PëPjC†PIP°P»P° C, PsC, P°C†PëC, PëPSC-P± Cr PrPsP·C- 5 PjPi PrPIP° C¶P°P·Pë PSP° PrPsP±C† (185 PíP°C†C-C" PSC, C-PI), CÍC, P°PSPsPIPëP»P° 27,6 %, P° PI PiC¶C†PíC- PíP»P°C†PµP±Ps (187 PíP°C†C-C" PSC, C-PI) C†PµPNë PíPsPeP°P·PSPëPe CÍC, P°PSPsPIPëPI 23,0 %. P—PiC-PrPSPs P· PsP±B¶ C"PrPSP°PSPëPjPë PrP°PSPëPjPë P· PeP»C-PSC-C†PSPëC... PrPsCÍP»C-PrP¶PµPSC¶ C, P°P·Pë 2 C, P° C, P°P·Pë 3, Cr 316 PíP°C†C-C" PSC, C-PI, C¶PeC- PsC, C¶PëPjC†PIP°P»Pë C, PsC, P°C†PëC, PëPSC-P± Cr PrPsP·C- 5 PjPi PrPIP° C¶P°P·Pë PSP° PrPsP±C† PíC¶PsC, C¶PiPsPj 48 C, PëP¶PSC-PI, C†P°CÍC, PsC, P° PIPëPSPëPePSPµPSPSC¶ C-PSC, µPeC†C-PNë CÍC, P°PSPsPIPëP»P° 35,1 %.

P'PëC¶P°P·PePsPIPëPNë PePsP»C-C,

PJ C¶P°PSPPrPsPjC-P·PsPIP°PSPëC... 8-C, PëP¶PSPµPIPëC... PrPsCÍP»C-PrP¶PµPSPSC¶C... C, P°P·Pë 2 C, P° C, P°P·Pë 3 C-PSPrC†PeC†C-PNëPSPsC— C, µC¶P°PíC-C— C†P°CÍC, PeP° PíP°C†C-C" PSC, C-PI, Cr C¶PePëC... PIPëPSPëPeP°P»Pë C-PSC, µPeC†C-C—, CÍC, P°PSPsPIPëP»P° 21,1 % (198 PíP°C†C-C" PSC, C-PI) Cr PiC¶C†PíC-, C¶PeP° PsC, C¶PëPjC†PIP°P»P° C, PsC, P°C†PëC, PëPSC-P± Cr PrPsP·C- 10 PjPi PrPIP° C¶P°P·Pë PSP° PrPsP±C† PíPsC¶C-PIPSC¶PSPs P· 15,2 % (43 PíP°C†C-C" PSC, Pë) Cr PiC¶C†PíC- PíP»P°C†PµP±Ps. PJ C¶P°PSPPrPsPjC-P·PsPIP°PSPsPjC† 52-C, PëP¶PSPµPIPpsPjC† PrPsCÍP»C-PrP¶PµPSPSC- C, P°P·Pë 3 PíC-PrC, C¶PëPjC†PIP°P»C¶PSPsC— C, µC¶P°PíC-C— C†P°CÍC, PeP° PíP°C†C-C" PSC, C-PI, Cr C¶PePëC... PIPëPSPëPeP°P»Pë C-PSC, µPeC†C-C—, CÍC, P°PSPsPIPëP»P° 35,9 % (71 PíP°C†C-C" PSC,) Cr PiC¶C†PíC-, C¶PeP° PsC, C¶PëPjC†B- PIP°P»P° C, PsC, P°C†PëC, PëPSC-P± Cr PrPsP·C- 5 PjPi PrPIP° C¶P°P·Pë PSP° PrPsP±C†, C- 39,8 % (78 PíP°C†C-C" PSC, C-PI) Cr PiC¶C†PíC-, C¶PeP° PsC, C¶PëPjC†PIP°P»P° C, PsC, P°C†PëC, PëPSC-P± Cr PrPsP·C- 10 PjPi PrPIP° C¶P°P·Pë PSP° PrPsP±C†, PíPsC¶C-PIPSC¶PSPs P· 24,2 % (48 PíP°C†C-C" PSC, C-PI) Cr PiC¶C†PíC- PíP»P°C†PµP±Ps.

P—P° PIPµCÍC¶ PíPµC¶C-PsPr C, µC¶P°PíC-C— C, PsC, P°C†PëC, PëPSC-P±PsPj PSP°PNëC†P°CÍC, C-C¶Pµ PíPsPIC-PrPsPjP»C¶P»PsCÍC¶ PíC¶Ps PSP°P·PsC, P°C¶PëPSPiC-C,, C¶PePëPNë P±C†PI P·P°C¶PµC" CÍC, C¶PsPIP°PSPëPNë Cr 18,2 % PíP°C†C-C" PSC, C-PI (211 PíP°C†C-C" PSC, C-PI).

P—P° PIPµCÍC¶ C†P°CÍ C, µC¶P°PíC-C— C, PsC, P°C†PëC, PëPSC-P±PsPj Cr C†C¶PsPjC† PrPsCÍP»C-PrP¶PµPSPSC- P·P°PíP°P»C¶PSP° C†P°CÍC, PsC, P° PIPëPSPëPePSPµPSPSC¶ C-PSC, µPeC†C-PNë CÍC, P°PSPsPIPëP»P° 60,3 C¶PIPëC%P° PSP° 100 PíP°C†C-C" PSC, Ps- C¶PsPeC-PI (Cr 49,4 % PíP°C†C-C" PSC, C-PI; P·P°PíP°P»PsPj Cr 572 PíP°C†C-C" PSC, C-PI).

PŸPµC¶PNëPsP·PSC- C-PSC, µPeC†C-C—

P PµPIPjP°C, PsC—PrPSPëPNë P°C¶C, C¶PëC,

PJ 6-PjC-CÍC¶C†PSPëC... C- 24-PjC-CÍC¶C†PSPëC... PePsPSC, C¶PsP»C¶PsPIP°PSPëC... PeP»C-PSC-C†PSPëC... PrPsCÍP»C-PrP¶PµPSPSC¶C... C†P°CÍC, PsC, P° PIPëPSPëPePSPµPSPSC¶ CÍPµC¶PNëPsP·PSPëC... C-PSC, µPeC†C-PNë Cr PiC¶C†PíC- PjPsPSPsC, µC¶P°PíC-C— C, PsC, P°C†PëC, PëPSC-P±PsPj Cr PrPsP·C- 5 PjPi PrPIP° C¶P°P·Pë PSP° PrPsP±C† CÍC, P°PSPsPIPëP»P° 1,7 PíP°C†C-C" PSC, P° P· PIC-PrPíPsPIC-PrPSPëPjPë C¶PIPëC%P°PjPë PSP° 100 PíP°C†C-C" PSC, Ps-C¶PsPeC-PI. PJ PiC¶C†PíC- PjPsPSPsC, µC¶P°PíC-C— C, PsC, P°C†PëC, PëPSC-P±PsPj Cr PrPsP·C- 10 PjPi PrPIP° C¶P°P·Pë PSP° PrPsP±C† C†P°CÍC, PsC, P° PIPëPSPëPePSPµPSPSC¶ PIC-PrPíPsPIC-PrPSPëC... C¶PIPëC% CÍC, P°PSPsPIPëP»P° 1,6 PíP°C†C-C" PSC, P° PSP° 100 PíP°C†C-C" PSC, Ps-C¶PsPeC-PI; Cr PiC¶C†PíC- PíP»P°C†PµP±Ps C†C¶ C†P°CÍC, PsC, P° CÍC, P°PSPsPIPëP»P° 0 C¶PIPëC% PSP° 100 PíP°C†C-C" PSC, Ps-C¶PsPeC-PI, P° PI PiC¶C†PíC- P¶PŸP¶ B¶ 1,9 PíP°C†C-C" PSC, P° P·

PIC-PrPīPsPIC-PrPSPēPjPē CĪPIPēC%P°PjPē PSP° 100 PīP°C†C-C"PSC,Ps-CĤPsPeC-PI.

PJ PrPsCīP»C-PrP¶PμPSPSCĪC... C,CĤPēPIP°P»C-CīC,CĤ 6, 12 P°P±Ps 24 PjC-CīCĪC†C-C†P°CīC,PsC,P° PIPēPSPēPePSPμPSPSCĪ CīPμCĤPNēPsP·PSPēC... C-PSC,,PμPeC†C-PNē Cr PiCĤCrPīP°C..., CĪPeC- PsC,CĤPēPjCrPIP°P»Pē C,PsC,,P°C†PēC,PēPSC-P± Cr PrPsP·C- 5 PjPi PrPIP° CĤP°P·Pē PSP° PrPsP±Cr PNē 10 PjPi PrPIP° CĤP°P·Pē PSP° PrPsP±Cr PīP»CĤCī DMARD, CīC,P°PSPsPIPēP»P° 3,6 C- 3,4 PīP°C†C-C"PSC,P° P· PIC-PrPīPsPIC-PrPSPēPjPē CĪPIPēC%P°PjPē PSP° 100 PīP°C†C-C"PSC,Ps-CĤPsPeC-PI PIC-PrPīPsPIC-PrPSPs PīPsCĤC-PIPSĪPSPs P· 1,7 PīP°C†C-C"PSC,P° P· PIC-PrPīPsPIC-PrPSPēPjPē CĪPIPēC%P°PjPē PSP° 100 PīP°C†C-C"PSC,Ps-CĤPsPeC-PI Cr PiCĤCrPiC- PīP»P°C†PμP±Ps PīP»CĤCī DMARD.

PJ PīPsPīCrP»CĪC†C-C— PrP»CĪ PsC†C-PSCĤPIP°PSPSCĪ PrPsPIPīPsCīC,CĤPsPePsPIPisC— P±PμP·PīPμPePē, PrPs CĪPePsC— PIPeP»CĤC†P°P»Pē PīP°C†C-C"PSC,C-PI, C%Ps PsC,CĤPēPjCrPIP°P»Pē C,PsC,,P°C†PēC,PēPSC-P± P·P° PICīC-PjP° CīC...PIP°P»PμPSPēPjPē PīPsPeP°P·P°PSPSCĪPjPē, P·P°PīP°P»CĤPSP° C†P°CīC,PsC,P° PIPēPSPēPePSPμPSPSCĪ CīPμCĤPNēPsP·PSPēC... C-PSC,,PμPeC†C-PNē CīC,P°PSPsPIPēP»P° 2,4 C- 3,0 PīP°C†C-C"PSC,P° P· PIC-PrPīPsPIC-PrPSPēPjPē CĪPIPēC%P°PjPē PSP° 100 PīP°C†C-C"PSC,Ps-CĤPsPeC-PI PrP»CĪ PiCĤCrPī C,PsC,,P°C†PēC,PēPSC-P±Cr PI PrPsP·P°C... 5 PjPi C- 10 PjPi PrPIP° CĤP°P·Pē PSP° PrPsP±Cr PIC-PrPīPsPIC-PrPSPs. P"Ps PSP°PNēC†P°CīC,C-CēPēC... CīPμCĤPNēPsP·PSPēC... C-PSC,,PμPeC†C-PNē PSP°P»PμP¶P°P»Pē PīPSPμPIPjPsPSC-CĪ, PsPīPμCĤC-P·CrCĤC†PēPNē PīPμCĤPīPμCī, C-PSC,,PμPeC†C-C— CīPμC†PsPIPēPIC-PrPSPēC... CēP»CĪC...C-PI, C,,P»PμPiPjPsPSP°, PīP°CīC,CĤPsPμPSC,PμCĤPēC, C- PrPēPIPμCĤC,PēPeCrP»C-C,, PμPsPIC-PrPsPjP»CĪP»PsCīCĪ PiCĤPs PIPēPīP°PrPePē PIPēPSPēPePSPμPSPSCĪ PsPīPsCĤC,CrPSC-CīC,PēC†PSPēC... C-PSC,,PμPeC†C-PNē (PrPēPI. CĤPsP·PrC-P» B«PhCīPsP±P»PēPIPsCīC,C- P·P°CīC,PsCīCrPIP°PSPSCĪB»).

PJ PIPμP»PēPePsPjCr (N 4362) CĤP°PSPPrPsPjC-P·PsPIP°PSPsPjCr PīC-CīP»CĪCĤPμC"CīC,CĤP°C†C-PNēPSPsPjCr PrPsCīP»C-PrP¶PμPSPSC- P±PμP·PīPμPePē P·P° CrC†P°CīC,CĤ PīP°C†C-C"PSC,C-PI P· P Ph PIC-PePsPj PIC-Pr 50 CĤPsPeC-PI P· PīCĤPēPSP°PNēPjPSC- PsPrPSPēPj PrPsPrP°C,PePsPIPēPj CīPμCĤC†PμPIPs-CīCrPrPēPSPSPēPj C,,P°PeC,PsCĤPsPj CĤPēP·PēPeCr CīPīPsCīC,PμCĤC-PiP°P»PsCīCĪ PrPsP·PsP·P°P»PμP¶PSPμ P·P±C-P»CĤCēPμPSPSCĪ CīPμCĤPNēPsP·PSPēC... C-PSC,,PμPeC†C-PNē PīCĤPē P·P°CīC,PsCīCrPIP°PSPSC- C,PsC,,P°C†PēC,PēPSC-P±Cr PīPsCĤC-PIPSĪPSPs P· PIC-PrPīPsPIC-PrPSPēPj PīPsPeP°P·PSPēPePsPj PīCĤPē P·P°CīC,PsCīCrPIP°PSPSC- C-PSPiC-P±C-C,PsCĤC-PI PαPκPμ (PrPēPI. CĤPsP·PrC-P» B«PhCīPsP±P»PēPIPsCīC,C- P·P°CīC,PsCīCrPIP°PSPSCĪB»). PšP°CīC,PsC,P° PIPēPSPēPePSPμPSPSCĪ (P· 95%-Pj P"Pt) CīPμCĤPNēPsP·PSPēC... C-PSC,,PμPeC†C-PNē Cr PiCĤCrPīC- C,PsC,,P°C†PēC,PēPSC-P±Cr 5 PjPi PrPIP° CĤP°P·Pē PSP° PrPsP±Cr, C,PsC,,P°C†PēC,PēPSC-P±Cr 10 PjPi PrPIP° CĤP°P·Pē PSP° PrPsP±Cr C,P° C-PSPiC-P±C-C,PsCĤC-PI PαPκPμ CīC,P°PSPsPIPēP»P° 2,86 (2,41; 3,37), 3,64 (3,11; 4,23) C,P° 2,44 (2,02; 2,92) PIPēPīP°PrPeCr PSP° 100 PīP°C†C-C"PSC,Ps-CĤPsPeC-PI PIC-PrPīPsPIC-PrPSPs. P'C-PrPSPsCēPμPSPSCĪ CĤPēP·PēPeC-PI CīPμCĤPNēPsP·PSPēC... C-PSC,,PμPeC†C-PNē PīCĤPē P·P°CīC,PsCīCrPIP°PSPSC- C,PsC,,P°C†PēC,PēPSC-P±Cr 10 PjPi PrPIP° CĤP°P·Pē PSP° PrPsP±Cr C- C,PsC,,P°C†PēC,PēPSC-P±Cr 5 PjPi PrPIP° CĤP°P·Pē PSP° PrPsP±Cr PīPsCĤC-PIPSĪPSPs P· C-PαPκPμ CīC,P°PSPsPIPēP»Ps 1,17 (0,92; 1,50) C- 1,48 (1,17; 1,87) PIC-PrPīPsPIC-PrPSPs.

PhPSPeC-P»PsP·CžCĤC†PēPNē CīPīPsPSPPrPēP»C-C,

P—PiC-PrPSPs P· PsP±BĤ™C"PrPSP°PSPēPjPē PrP°PSPēPjPē P· PeP»C-PSC-C†PSPēC... PrPsCīP»C-PrP¶PμPSCĤ C,,P°P·Pē 2 C,P° C,,P°P·Pē 3, PSP° 316 PīP°C†C-C"PSC,C-PI, CĪPeC- PsC,CĤPēPjCrPIP°P»Pē C,PsC,,P°C†PēC,PēPSC-P± Cr PrPsP·C- 5 PjPi PrPIP° CĤP°P·Pē PSP° PrPsP±Cr PīCĤPsC,CĪPiPsPj PīPμCĤC-PsPrCr PrPs 48 C,PēP¶PSC-PI, P±CrPI

P·P°CḡPμC"ĆĲC, CḡPsPIP°PSPēPNē PsPrPēPS PIPēPīP°PrPsPe CĲPμCḡPNēPsP·PSPsC—
C-PSC,,PμPeC†C-C— (P°CĲPμPīC,PēC†PSPēPNē PjPμPSC-PSPiC-C,), C,PsP±C,Ps PīPsPeP°P·PSPēPe
C†P°CĲC,PsC,Pē CĲC,P°PSPsPIPēPI 0,43 PīP°C†C-C"PS C,P° P· PIC-PrPīPsPIC-PrPSPēPjPē
CĲPIPēC%P°PjPē PSP° 100 PīP°C†C-C"PS C,Ps-CḡPsPeC-PI.

P'PēCḡP°P·PePsPIPēPNē PePsP»C-C,

PŠP°CĲC,PsC,P° PIPēPSPēPePSPμPSPSCĲ C- PIPēPrPē CĲPμCḡPNēPsP·PSPēC...
C-PSC,,PμPeC†C-PNē, P·P°CḡPμC"ĆĲC, CḡPsPIP°PSPēC... CĲ PeP»C-PSC-C†PSPēC...
PrPsCĲP»C-PrP¶PμPSPSCĲC... C%PsPrPs PīPsPeP°P·P°PSPSCĲ P'Pḡ, P·P°PīP°P»PsPj P±CĲP»Pē
PīPsPrC-P±PSC- PrPs C,PēC..., PīCḡPs CĲPeC- PīPsPIC-PrPsPjP»CĲP»PsCĲCĲ
PI PeP»C-PSC-C†PSPēC... PrPsCĲP»C-PrP¶PμPSPSCĲC... C%PsPrPs PīPsPeP°P·P°PSPSCĲ P Pḡ PI
PiCḡCĲPīP°C... PjPsPSPsC,PμCḡP°PīC-C— C,PsC,,P°C†PēC,PēPSC-P±PsPj.

PŸPμCḡPNēPsP·PSC- C-PSC,,PμPeC†C-C— PI PīP°C†C-C"PS C-C-PI PīPsC...PēP»PsPiPs PIC-PeCé

P†P· 4271 PīP°C†C-C"PS C,P°, CĲPeC- P±CḡP°P»Pē CĲC†P°CĲC,Cḡ CĲ
PrPsCĲP»C-PrP¶PμPSPSCĲC... Ibḡ"VI, P·P°PīP°P»PsPj 608 PīP°C†C-C"PS C-C-PI C-P· P Pḡ
P±CĲP»Pē PIC-PePsPj 65 CḡPsPeC-PI C- CĲC,P°CḡCēPμ, CĲ C†CḡPsPjCĲ C†PēCĲP»C- P±CĲP»Pē
85 PīP°C†C-C"PS C-C-PI PIC-PePsPj 75 CḡPsPeC-PI C- CĲC,P°CḡCēPμ. PŠP°CĲC,PsC,P°
PIPēPSPēPePSPμPSPSCĲ CĲPμCḡPNēPsP·PSPēC... C-PSC,,PμPeC†C-PNē CĲPμCḡPμPr
PīP°C†C-C"PS C-C-PI PIC-PePsPj 65 CḡPsPeC-PI C- CĲC,P°CḡCēPμ, CĲPeC-
PsC,CḡPēPjCĲPīP°P»Pē C,PsC,,P°C†PēC,PēPSC-P±, P±CĲP»P° PIPēC%PsCḡ, PSC-P¶ CĲ
PīP°C†C-C"PS C-C-PI PIC-PePsPj PjPsP»PsPrCēPμ 65 CḡPsPeC-PI (4,8 PSP° 100 PīP°C†C-C"PS C,Ps-
CḡPsPeC-PI PīPsCḡC-PIPSĲPSPs P· 2,4 PSP° 100 PīP°C†C-C"PS C,Ps-CḡPsPeC-PI
PIC-PrPīPsPIC-PrPSPs).

PJ PIPμP»PēPePsPjCĲ (N = 4362) CḡP°PSPrPsPjC-P·PsPIP°PSPsPjCĲ
PīC-CĲP»CĲCḡPμC"ĆĲC, CḡP°C†C-PNēPSPsPjCĲ PrPsCĲP»C-PrP¶PμPSPSC- P±PμP·PīPμPePē P·P°
CĲC†P°CĲC,Cḡ PīP°C†C-C"PS C-C-PI P· P Pḡ PIC-PePsPj PIC-Pr 50 CḡPsPeC-PI P·
PīCḡPēPSP°PNēPjPSC- PsPrPSPēPj PrPsPrP°C,PePsPIPēPj CĲPμCḡC†PμPIPs-CĲCĲPrPēPSPSPēPj
C,,P°PeC,PsCḡPsPj CḡPēP·PēPeCĲ CĲPīPsCĲC,PμCḡC-PiP°P»PsCĲCĲ P·P±C-P»CḡCēPμPSPSCĲ
CĲPμCḡPNēPsP·PSPēC... C-PSC,,PμPeC†C-PNē CĲ PīP°C†C-C"PS C-C-PI PIC-PePsPj PIC-Pr 65
CḡPsPeC-PI PīCḡPē P·P°CĲC,PsCĲCĲPīP°PSPSC- C,PsC,,P°C†PēC,PēPSC-P±CĲ 10 PjPi PrPIP°
CḡP°P·Pē PSP° PrPsP±CĲ PīPsCḡC-PIPSĲPSPs P· PIC-PrPīPsPIC-PrPSPēPj
PīPsPeP°P·PSPēPePsPj PīCḡPē P·P°CĲC,PsCĲCĲPīP°PSPSC- C-PSPiC-P±C-C,PsCḡC-PI PαPḡPμ
P°P±Ps C,PsC,,P°C†PēC,PēPSC-P±CĲ 5 PjPi PrPIP° CḡP°P·Pē PSP° PrPsP±CĲ (PrPēPI.
CḡPsP·PrC-P» B«PḡCĲPsP±P»PēPIPsCĲC,C- P·P°CĲC,PsCĲCĲPīP°PSPSCĲB»). PŠP°CĲC,PsC,P°
PIPēPSPēPePSPμPSPSCĲB (P· 95%-Pj P"P†) CĲPμCḡPNēPsP·PSPēC... C-PSC,,PμPeC†C-PNē CĲ
PīP°C†C-C"PS C-C-PI PIC-PePsPj PIC-Pr 65 CḡPsPeC-PI CĲ PiCḡCĲPīC-
C,PsC,,P°C†PēC,PēPSC-P±CĲ 5 PjPi PrPIP° CḡP°P·Pē PSP° PrPsP±CĲ, C,PsC,,P°C†PēC,PēPSC-P±CĲ
10 PjPi PrPIP° CḡP°P·Pē PSP° PrPsP±CĲ C,P° C-PαPḡPμ CĲC,P°PSPsPIPēP»P° 4,03 (3,02; 5,27),
5,85 (4,64; 7,30) C- 3,73 (2,81; 4,85) PIPēPīP°PrPeCĲ PSP° 100 PīP°C†C-C"PS C,Ps-CḡPsPeC-PI
PIC-PrPīPsPIC-PrPSPs).

P'C-PrPSPsCēPμPSPSCĲ CḡPēP·PēPeC-PI CĲPμCḡPNēPsP·PSPēC... C-PSC,,PμPeC†C-PNē CĲ
PīP°C†C-C"PS C-C-PI PIC-PePsPj PIC-Pr 65 CḡPsPeC-PI PīCḡPē P·P°CĲC,PsCĲCĲPīP°PSPSC-
C,PsC,,P°C†PēC,PēPSC-P±CĲ 5 PjPi PrPIP° CḡP°P·Pē PSP° PrPsP±CĲ C-
C,PsC,,P°C†PēC,PēPSC-P±CĲ 10 PjPi PrP»CĲ PrPIP° CḡP°P·Pē PSP° PrPsP±CĲ
PīPsCḡC-PIPSĲPSPs P· C-PSPiC-P±C-C,PsCḡP°PjPē PαPḡPμ CĲC,P°PSPsPIPēP»Ps 1,08 (0,74,
1,58) C- 1,55 (1,10, 2,19) PIC-PrPīPsPIC-PrPSPs.

PIPëPİP°PrPeC-PI PsPİPµCḡC-P·CfCḡC±PsPiPs PiPµCḡPİPµCfCf Cr PiCḡCfPİC-
P·P°CfC,PsCfCfPIP°PSPSCİ C,PsC,,P°C†PëC,PëPSC-P±Cf PİPsCḡC-PIPSCİPSPs P· C,P°PePëPjPë
Cf PiCḡCfPİC- P·P°CfC,PsCfCfPIP°PSPSCİ C-P±P±Pµ. PŞP°CfC,PsC,P° PIPëPSPëPePSPµPSPSCİ
(95%-PNë P"P†) PsPİPµCḡC-P·CfCḡC±PsPiPs PiPµCḡPİPµCfCf PI PiCḡCfPİC-
C,PsC,,P°C†PëC,PëPSC-P±Cf PI PrPsP·C- 5 PjPi PrPIP° CḡP°P·Pë PSP° PrPsP±Cf,
C,PsC,,P°C†PëC,PëPSC-P±Cf 10 PjPi PrPIP° CḡP°P·Pë PSP° PrPsP±Cf PNë
C-PSPİC-P±C-C,PsCḡC-PI P±P±Pµ CfC,P°PSPsPIPëP»P° 3,75 (3,22; 4,34), 3,94 (3,38; 4,57) C- 1,18
(0,90; 1,52) PIPëPİP°PrPeCf PSP° 100 PİP°C†C-C"PSC,Ps-CḡPsPeC-PI PIC-PrPİPsPIC-PrPSPs.

P>P°P±PsCḡP°C,PsCḡPSC- P°PSP°P»C-P·Pë

P>C-PjC,,PsC†PëC,Pë

Pj PePsPSC,CḡPsP»CHPsPIP°PSPëC... PeP»C-PSC-C±PSPëC... PrPsCfP»C-PrP¶PµPSPSCİC... C-P·
PIPëPIC±PµPSPSCİ PİPsPeP°P·P°PSPSCİ P Ph PİC-PrC,PIPµCḡPrP¶PµPSPµ P·PSPëP¶PµPSPSCİ
PhPµP» PjPµPSC€Pµ 500 PeP»C-C,PëPS/PjPj³ CfPİPsCfC,PµCḡC-PİP°P»PsCfCİ PI 0,3 %
PİP°C†C-C"PSC,C-PI, P° PhPµP» Cf PrC-P°PİP°P·PsPSC- PjC-P¶ 500
C- 750 PeP»C-C,PëPS/PjPj³ бґ " Cf 1,9 % PİP°C†C-C"PSC,C-PI P· PsP±бґ™C"PrPSP°PSPsC—
PİPsPİCfP»CİC†C-C— PİP°C†C-C"PSC,C-PI, CİPeC- PsC,CḡPëPjCfPIP°P»Pë PrPsP·Pë 5 PjPi
PrPIP° CḡP°P·Pë PSP° PrPsP±Cf C,P° 10 PjPi PrPIP° CḡP°P·Pë PSP° PrPsP±Cf.

Pj PİPsPİCfP»CİC†C-C— PrP»Cİ PsC†C-PSPëPë PrPsPIPiPsCfC,CḡPsPePsPIPsC—
P±PµP·PİPµPePë PI PİP°C†C-C"PSC,C-PI C-P· P Ph PİC-PrC,PIPµCḡPrP¶PµPSPµ
P·PSPëP¶PµPSPSCİ PhPµP» PrPs CḡC-PIPSCİ PjPµPSC€Pµ 500 PeP»C-C,PëPS/PjPj³
CfPİPsCfC,PµCḡC-PİP°P»PsCfCİ PI 1,3 % PİP°C†C-C"PSC,C-PI, P° PhPµP» Cf
PrC-P°PİP°P·PsPSC- PjC-P¶ 500 C- 750 PeP»C-C,PëPS/PjPj³ бґ " Cf 8,4 % PİP°C†C-C"PSC,C-PI P·
PsP±бґ™C"PrPSP°PSPsC— PİPsPİCfP»CİC†C-C— PİP°C†C-C"PSC,C-PI, CİPeC-
PsC,CḡPëPjCfPIP°P»Pë PrPsP·Pë 5 PjPi PrPIP° CḡP°P·Pë PSP° PrPsP±Cf C,P° 10 PjPi PrPIP°
CḡP°P·Pë PSP° PrPsP±Cf.

PµC-PrC,PIPµCḡPrP¶PµPSP° PhPµP» PjPµPSC€Pµ 750 PeP»C-C,PëPS/PjPj³ P±CfP»P°
P°CfPsC†C-PNëPsPIP°PSP° P· PİC-PrPIPëC%PµPSPsCḡ C±P°CfC,PsC,PsCḡ
PIPëPSPëPePSPµPSPSCİ CfPµCḡPNëPsP·PSPëC... C-PSC,,PµPeC†C-PNë (PrPëPI.
CḡPsP·PrC-P» B«PhCfPsP±P»PëPIPsCfC,C- P·P°CfC,PsCfCfPIP°PSPSCİB»).

Pj PeP»C-PSC-C±PSPëC... PrPsCfP»C-PrP¶PµPSPSCİC... C%PsPrPs PİPsPeP°P·P°PSPSCİ P'Pµ
P·PjC-PSPë PI PhPµP», C%Ps CfPİPsCfC,PµCḡC-PİP°P»PëCfCİ PİC-Pr C±P°Cf
P»C-PeCfPIP°PSPSCİ C,PsC,,P°C†PëC,PëPSC-P±PsPj, P±CfP»Pë P°PSP°P»PsPiC-C±PSC- PrPs
P·PjC-PS, CİPeC- PIC-PrPjC-C±P°P»PëCfCİ PI PeP»C-PSC-C±PSPëC...
PrPsCfP»C-PrP¶PµPSPSCİC... C%PsPrPs PİPsPeP°P·P°PSPSCİ P Ph.

P±PµPNëC,CḡPsC,,C-P»Pë

Pj PePsPSC,CḡPsP»CHPsPIP°PSPëC... PeP»C-PSC-C±PSPëC... PrPsCfP»C-PrP¶PµPSPSCİC... C-P·
PIPëPIC±PµPSPSCİ PİPsPeP°P·P°PSPSCİ P Ph PİC-PrC,PIPµCḡPrP¶PµPSPµ P·PSPëP¶PµPSPSCİ
PhPµP± PrPs P·PSP°C±PµPSCḡ PjPµPSC€Pµ 1000 PeP»C-C,PëPS/PjPj³
CfPİPsCfC,PµCḡC-PİP°P»PsCfCİ PI 0,08 % PİP°C†C-C"PSC,C-PI P· PsP±бґ™C"PrPSP°PSPsC—
PİPsPİCfP»CİC†C-C— PİP°C†C-C"PSC,C-PI, CİPeC- PsC,CḡPëPjCfPIP°P»Pë PrPsP·Pë 5 PjPi
PrPIP° CḡP°P·Pë PSP° PrPsP±Cf C,P° 10 PjPi PrPIP° CḡP°P·Pë PSP° PrPsP±Cf.
PµC-PrC,PIPµCḡPrP¶PµPSPsPiPs P·PSPëP¶PµPSPSCİ PhPµP± PrPs CḡC-PIPSCİ PjPµPSC€Pµ
500 PeP»C-C,PëPS/PjPj³ PSPµ PIC-PrPjC-C±P°P»PsCfCİ PI P¶PsPrPSC-PNë PiCḡCfPİC-
C,PµCḡP°PİC-C—. PŞC-C,PePsPiPs P·PIбґ™ CİP·PeCf PjC-P¶ PSPµPNëC,CḡPsPİPµPSC-C"Cḡ C,P°

PIPëPSPëPePSPµPSPSCΠPj CΓPµCḡPNεPsP·PSPëC... C-PSC,,PµPeC†C-PNε PSPµ P±C†P»Ps.

PJ PīPsPīC†P»CΠC†C-C— PrP»CΠ PsC†C-PSPëPë PrPsPIPiPsC†C,CḡPsPePsPIPsC—
P±PµP·PīPµPePë PI PīP°C†C-C''PSC,C-PI C-P· P Ph C...P°CḡP°PeC,PµCḡ C- C†P°C†C,PsC,P°
PIPëPSPëPePSPµPSPSCΠ PīC-PrC,PIPµCḡPrP¶PµPSPsPiPs P·PSPëP¶PµPSPSCΠ PhPḡPḡ
P·P°P»PëCεP°P»PëC†CΠ PSP° C,PsPjC† CΓP°PjPsPjC† CḡC-PIPSC-, CΠPePëPNε
CΓPīPsC†C,PµCḡC-PiP°PIC†CΠ PI PePsPSC,CḡPsP»CHPsPIP°PSPëC... PeP»C-PSC-C†PSPëC...
PrPsC†P»C-PrP¶PµPSPSCΠC... (PrPëPI. CḡPsP·PrC-P» B«PhC†PsP±P»PëPIPsC†C,C-
P·P°C†C,PsC†C†PIP°PSPSCΠB»).

PJ PeP»C-PSC-C†PSPëC... PrPsC†P»C-PrP¶PµPSPSCΠC... C%PsPrPs PīPsPeP°P·P°PSPSCΠ B P'ḡ
P·PjC-PSPë PI PhPḡPḡ, C%Ps CΓPīPsC†C,PµCḡC-PiP°P»PëC†CΠ PīC-Pr C†P°C†
P»C-PeC†PIP°PSPSCΠ C,PsC,,P°C†PëC,PëPSC-P±PsPj, P±C†P»Pë P°PSP°P»PsPiC-C†PSC- PrPs
P·PjC-PS, CΠPeC- PIC-PrPjC-C†P°P»PëC†CΠ PI PeP»C-PSC-C†PSPëC...
PrPsC†P»C-PrP¶PµPSPSCΠC... C%PsPrPs PīPsPeP°P·P°PSPSCΠ P Ph.

PjCḡPsPjP±PsC†PëC,Pë

PJ PePsPSC,CḡPsP»CHPsPIP°PSPëC... PeP»C-PSC-C†PSPëC... PrPsC†P»C-PrP¶PµPSPSCΠC...
C,,P°P·Pë 3 (C%PsPrPs PīPsPeP°P·P°PSCḡ P Ph, PµC†Ph, PhPḡ, P'ḡ) PrPs C†C†P°C†C,C-
PrPsPīC†C†PeP°P»PëC†CΠ P»PëCεPµ PīP°C†C-C''PSC,Pë P· PeC-P»CHPeC-C†C,Cḡ
C,CḡPsPjP±PsC†PëC,C-PI ≥ 100 000 PeP»C-C,PëPS/PjPj³, C,PsPjC† PSP°CḡP°P·C- PSPµPjP°C''
C-PSC,,PsCḡPjP°C†C-C— C%PsPrPs P·P°C†C,PsC†C†PIP°PSPSCΠ C,PsC,,P°C†PëC,PëPSC-P±C†
PīP°C†C-C''PSC,P°Pj C-P· PeC-P»CHPeC-C†C,Cḡ C,CḡPsPjP±PsC†PëC,C-PI
< 100 000 PeP»C-C,PëPS/PjPj³ PrPs PīPsC†P°C,PeC† C,PµCḡP°PīC-C—
C,PsC,,P°C†PëC,PëPSC-P±PsPj.

PµPµC†C-PSPëPsPIC- C,,PµCḡPjPµPSC,Pë

PµC-PrC,PIPµCḡPrP¶PµPSC- PIPëPīP°PrPePë PīC-PrPIPëC%PµPSPSCΠ CḡC-PIPSCΠ
PīPµC†C-PSPëPsPIPëC... C,,PµCḡPjPµPSC,C-PI C† C,CḡPë CḡP°P·Pë PIPëC%Pµ
PIPµCḡC...PSCḡPsC— PjPµP¶C- PSPsCḡPjPë (3 × P'ḡPḡ) C† PīP°C†C-C''PSC,C-PI C-P· P Ph
CΓPīPsC†C,PµCḡC-PiP°P»PëC†CΠ CḡC-PrPePs. PJ PīP°C†C-C''PSC,C-PI, C† CΠPePëC...
CΓPīPsC†C,PµCḡC-PiP°P»PsC†CΠ PīC-PrPIPëC%PµPSPSCΠ CḡC-PIPSC-PI
PīPµC†C-PSPëPsPIPëC... C,,PµCḡPjPµPSC,C-PI, P·PjC-PSP° C†C...PµPjPë C,PµCḡP°PīC-C—
(PSP°PīCḡPëPeP»P°Pr, P·PjPµPSCεPµPSPSCΠ PrPsP·Pë C†C†PīC†C,PSCHPsPiPs DMARD,
PīCḡPëP·C†PīPëPSPµPSPSCΠ P·P°C†C,PsC†C†PIP°PSPSCΠ C,PsC,,P°C†PëC,PëPSC-P±C† P°P±Ps
P·PSPëP¶PµPSPSCΠ PrPsP·Pë C,PsC,,P°C†PëC,PëPSC-P±C†) PrPsPīPsPjP°PīP°P»P°
P·PjPµPSCεPëC,Pë P°P±Ps PSPsCḡPjP°P»C-P·C†PIP°C,Pë CḡC-PIPSC- PīPµC†C-PSPëPsPIPëC...
C,,PµCḡPjPµPSC,C-PI.

PJ PePsPSC,CḡPsP»CHPsPIP°PSC-PNε C†P°C†C,PëPSC- PrPsC†P»C-PrP¶PµPSPSCΠ C,,P°P·Pë 3 P·
PIPëPIC†PµPSPSCΠ PjPsPSPsC,PµCḡP°PīC-C— PīCḡPë P Ph (0ḡḡ“3 PjC-C†CΠC†C-)
(PrPsC†P»C-PrP¶PµPSPSCΠ I) PīC-PrPIPëC%PµPSPSCΠ CḡC-PIPSCΠ PhP·Pḡ PrPs
P·PSP°C†PµPSCḡ PīPsPSP°Pr 3 × P'ḡPḡ CΓPīPsC†C,PµCḡC-PiP°P»PsC†CΠ PI 1,65 %, 0,41 % C-
0 % PīP°C†C-C''PSC,C-PI, CΠPeC- PsC,CḡPëPjC†PIP°P»Pë PīP»P°C†PµP±Ps,
C,PsC,,P°C†PëC,PëPSC-P± 5 PjPi C- C,PsC,,P°C†PëC,PëPSC-P± 10 PjPi PrPIP° CḡP°P·Pë PSP°
PrPsP±C† PIC-PrPīPsPIC-PrPSPs. PJ C†CHPsPjC† PrPsC†P»C-PrP¶PµPSPSC-
PīC-PrPIPëC%PµPSPSCΠ CḡC-PIPSCΠ PhPḡPḡ PrPs P·PSP°C†PµPSCḡ PīPsPSP°Pr 3 × P'ḡPḡ
CΓPīPsC†C,PµCḡC-PiP°P»PsC†CΠ PI 1,65 %, 0,41 % C- 0 % PīP°C†C-C''PSC,C-PI, CΠPeC-
PsC,CḡPëPjC†PIP°P»Pë PīP»P°C†PµP±Ps, C,PsC,,P°C†PëC,PëPSC-P± 5 PjPi C-
C,PsC,,P°C†PëC,PëPSC-P± 10 PjPi PrPIP° CḡP°P·Pë PSP° PrPsP±C† PIC-PrPīPsPIC-PrPSPs.

PJ PrPsCfP»C-PrP¶PµPSPSC- C,,P°P·Pë 3 P· PIPëPIC±PµPSPSC¶ PjPsPSPsC,PµC¶P°PïC-C—
 PïC¶Pë P Ph (0B¶“24 PjC-CfC¶C¶C-) (PrPsCfP»C-PrP¶PµPSPSC¶ VI) PïC-PrPIPëC%PµPSPSC¶
 C¶C-PIPSC¶ PhP·Pÿ PrPs P·PSP°C±PµPSCH PïPsPSP°Pr 3 × P'P¶P¶ PIC-PrPjC-C±P°P»PsCfC¶ PI
 7,1 %, 3,0 % C- 3,0 % PïP°C¶C-C”PSC,C-PI, C¶PeC- PsC,C¶PëPjCfPïP°P»Pë P¶PÿP¶,
 C,PsC,,P°C¶PëC,PëPSC-P± 5 PjPi C- C,PsC,,P°C¶PëC,PëPSC-P± 10 PjPi PrPIP° C¶P°P·Pë PSP°
 PrPsP±Cf PIC-PrPïPsPIC-PrPSPs. PJ C¶CHbPsPjCf PrPsCfP»C-PrP¶PµPSPSC-
 PïC-PrPIPëC%PµPSPSC¶ C¶C-PIPSC¶ PhPÿPÿ PrPs P·PSP°C±PµPSCH PïPsPSP°Pr 3 × P'P¶P¶
 C¶PïPsCfC,PµC¶C-BPïP°P»PsCfC¶ PI 3,3 %, 1,6 % C- 1,5 % PïP°C¶C-C”PSC,C-PI, C¶PeC-
 PsC,C¶PëPjCfPïP°P»Pë P¶PÿP¶, C,PsC,,P°C¶PëC,PëPSC-P± 5 PjPi C- 10 PjPi PrPIP° C¶P°P·Pë
 PSP° PrPsP±Cf PIC-PrPïPsPIC-PrPSPs.

PJ PePsPSC,C¶PsP»CHbPsPIP°PSC-PNë C±P°CfC,PëPSC- PrPsCfP»C-PrP¶PµPSCH C,,P°P·Pë 3 Cf
 PïP°C¶C-C”PSC,C-PI C-P· P Ph, C¶PeC- PsC,C¶PëPjCfPïP°P»Pë CfCfPïCfC,PSCH
 C,PµC¶P°PïC-C¶ DMARD (0B¶“3 PjC-CfC¶C¶C-) (PrPsCfP»C-PrP¶PµPSPSC¶ IIB¶“V),
 PïC-PrPIPëC%PµPSPSC¶ C¶C-PIPSC¶ PhP·Pÿ PrPs P·PSP°C±PµPSCH PïPsPSP°Pr 3 × P'P¶P¶
 PIC-PrPjC-C±P°P»PsCfC¶ PI 0,9 %, 1,24 % C- 1,14 % PïP°C¶C-C”PSC,C-PI, C¶PeC-
 PïC¶PëPNëPjP°P»Pë PïP°P°C¶PµP±Ps, C,PsC,,P°C¶PëC,PëPSC-P± 5 PjPi C- 10 PjPi PrPIP° C¶P°P·Pë
 PSP° PrPsP±Cf PIC-PrPïPsPIC-PrPSPs. PJ C¶PëC... PrPsCfP»C-PrP¶PµPSPSC¶C...
 PïC-PrPIPëC%PµPSPSC¶ C¶C-PIPSC¶ PhPÿPÿ PrPs P·PSP°C±PµPSCH PïPsPSP°Pr 3 × P'P¶P¶
 C¶PïPsCfC,PµC¶C-PïP°P»PsCfC¶ PI 0,72 %, 0,5 % C- 0,31 % PïP°C¶C-C”PSC,C-PI, C¶PeC-
 PsC,C¶PëPjCfPïP°P»Pë PïP°P°C¶PµP±Ps, C,PsC,,P°C¶PëC,PëPSC-P± 5 PjPi C-
 C,PsC,,P°C¶PëC,PëPSC-P± 10 PjPi PrPIP° C¶P°P·Pë PSP° PrPsP±Cf PIC-PrPïPsPIC-PrPSPs.

PJ PrPsPIPiScfC,C¶PsPePsPIPëC... PïPsPrPsPIP¶PµPSPëC... PrPsCfP»C-PrP¶PµPSPSC¶C... Cf
 PïP°C¶C-C”PSC,C-PI C-P· P Ph PïC¶Pë PjPsPSPsC,PµC¶P°PïC-C— PïC-PrPIPëC%PµPSPSC¶
 C¶C-PIPSC¶ PhP·Pÿ PrPs P·PSP°C±PµPSCH PïPsPSP°Pr 3 × P'P¶P¶ PIC-PrPjC-C±P°P»PsCfC¶ PI
 1,1 % C- 1,4 % PïP°C¶C-C”PSC,C-PI, C¶PeC- PsC,C¶PëPjCfPïP°P»Pë C,PsC,,P°C¶PëC,PëPSC-P±
 5 PjPi C- 10 PjPi PrPIP° C¶P°P·Pë PSP° PrPsP±Cf PIC-PrPïPsPIC-PrPSPs.
 PµC-PrPIPëC%PµPSPSC¶ C¶C-PIPSC¶ PhPÿPÿ PrPs P·PSP°C±PµPSCH PïPsPSP°Pr 3 × P'P¶P¶
 C¶PïPsCfC,PµC¶C-PïP°P»PsCfC¶ PI < 1,0 % PïP°C¶C-C”PSC,C-PI Cf PïC¶CfPïP°C...
 C,PsC,,P°C¶PëC,PëPSC-P±Cf 5 PjPi C- 10 PjPi PrPIP° C¶P°P·Pë PSP° PrPsP±Cf.

PJ PrPsPIPiScfC,C¶PsPePsPIPëC... PïPsPrPsPIP¶PµPSPëC... PrPsCfP»C-PrP¶PµPSPSC¶C... Cf
 PïP°C¶C-C”PSC,C-PI C-P· P Ph, C¶PeC- PsC,C¶PëPjCfPïP°P»Pë CfCfPïCfC,PSCH
 C,PµC¶P°PïC-C¶ DMARD, PïC-PrPIPëC%PµPSPSC¶ C¶C-PIPSC¶ PhP·Pÿ PrPs P·PSP°C±PµPSCH
 PïPsPSP°Pr 3 × P'P¶P¶ CfPïPsCfC,PµC¶C-PïP°P»PsCfC¶ PI 1,8 % C,P° 1,6 %
 PïP°C¶C-C”PSC,C-PI, C¶PeC- PsC,C¶PëPjCfPïP°P»Pë C,PsC,,P°C¶PëC,PëPSC-P± Cf PrPsP·P°C...
 5 PjPi C- 10 PjPi PrPIP° C¶P°P·Pë PSP° PrPsP±Cf PIC-PrPïPsPIC-PrPSPs.
 PµC-PrPIPëC%PµPSPSC¶ C¶C-PIPSC¶ PhPÿPÿ PrPs P·PSP°C±PµPSCH PïPsPSP°Pr 3 × P'P¶P¶
 C¶PïPsCfC,PµC¶C-PïP°P»PsCfC¶ PI < 1,0 % PïP°C¶C-C”PSC,C-PI Cf PïC¶CfPïP°C...
 C,PsC,,P°C¶PëC,PëPSC-P±Cf 5 PjPi C- 10 PjPi PrPIP° C¶P°P·Pë PSP° PrPsP±Cf.

PJ PIPµP»PëPePsPjCf (N = 4362) C¶P°PSPrPsPjC-P·PsPIP°PSPsPjCf
 PïC-CfP»C¶C¶PµC”CfC,C¶P°C¶C-PNëPSPsPjCf PrPsCfP»C-PrP¶PµPSPSC- P±PµP·PïPµPePë P·P°
 CfC±P°CfC,C¶ PïP°C¶C-C”PSC,C-PI C-P· P Ph PIC-PePsPj 50 C¶PsPeC-PI C- CfC,P°C¶C¶Pµ P·
 PïC¶PëPSP°PNëPjPSC- PsPrPSPëPj PrPsPrP°C,PePsPIPëPj C,,P°PeC,PsC¶PsPj C¶PëP·PëPeCf
 CfPµC¶C±PµPIPs-CfCfPrPëPSPSPëC... CfCfPeP»P°PrPSPµPSCH PïC-PrPIPëC%PµPSPSC¶
 P°PeC,PëIPSPsCfC,C- PhP·Pÿ PrPs P·PSP°C±PµPSCH 3 × P'P¶P¶ P°P±Ps PIPëC%PëC...
 CfPïPsCfC,PµC¶C-PïP°P»PsCfC¶ PI 6,01 %, 6,54 % C,P° 3,77 % PïP°C¶C-C”PSC,C-PI, C¶PeC-
 PsC,C¶PëPjCfPïP°P»Pë C,PsC,,P°C¶PëC,PëPSC-P± Cf PrPsP·C- 5 PjPi PrPIP° C¶P°P·Pë PSP°
 PrPsP±Cf, C,PsC,,P°C¶PëC,PëPSC-P± Cf PrPsP·C- 10 PjPi PrPIP° C¶P°P·Pë PSP° PrPsP±Cf
 P°P±Ps C-PSPiC-P±C-C,PsC¶Pë P¶P¶Pµ PIC-PrPïPsPIC-PrPSPs. PµC-PrPIPëC%PµPSPSC¶

P°PeC, PēPIPSsCfC, C- PḥPŸPŷ PrPs P·PSP°C†PμPSCḤ 3 × P'PḥPḱ P°P±Ps PIPēC%PēC...
CfPiPsCfC, PμCḥC-PiP°P»PsCfC C 3,21 %, 4,57 % C, P° 2,38 % PiP°C†C-C" PSC, C-PI, CμPeC-
PsC, CḥPēPjCfPIP°P»Pē C, PsC,, P°C†PēC, PēPSC-P± Cr PrPsP·C- 5 PjPi PrPIP° CḥP°P·Pē PSP°
PrPsP±Cf, C, PsC,, P°C†PēC, PēPSC-P± Cr PrPsP·C- 10 PjPi PrPIP° CḥP°P·Pē PSP° PrPsP±Cf
P°P±Ps C-PSPiC-P±C-C, PsCḥPē PḥPḱPḥ PIC-PrPiPsPIC-PrPSPs.

Pj PeP»C-PSC-C†PSPēC... PrPsCfP»C-PrP¶PμPSPSC C... C%PsPrPs PiPsPeP°P·P°PSPSC C P'Pḥ
P·PjC-PSPē CḥC-PIPS-C PI PiPμC†C-PSPePsPIPēC... C,, PμCḥPjPμPSC, C-PI, C%Ps
CfPiPsCfC, PμCḥC-PiP°P»PēCfC C PiC-Pr C†P°Cf P»C-PeCfPIP°PSPSC C
C, PsC,, P°C†PēC, PēPSC-P±PsPj, P±CfP»Pē P°PSP°P»PsPiC-C†PSC- PrPs P·PjC-PS, CμPeC-
PIC-PrPjC-C†P°P»PēCfC C PI PeP»C-PSC-C†PSPēC... PrPsCfP»C-PrP¶PμPSPSC C... C%PsPrPs
PiPsPeP°P·P°PSPSC C P Pḥ.

P>C-PiC-PrPē

Pj PePsPSC, CḥPsP»CḥPsPIP°PSPēC... PiPsPrPIC-PNēPSPēC... CfP»C-PiPēC...
PeP»C-PSC-C†PSPēC... PrPsCfP»C-PrP¶PμPSPSC C... P Pḥ PiPμCḥCēPēPNē
PjPsPSC-C, PsCḥPēPSPi PiC-PrPIPēC%PμPSPSC C CḥC-PIPS-C PI P»C-PiC-PrC-PI
(P·P°PiP°P»CḥPSPsPiPs C...PsP»PμCfC, PμCḥPēPSCf, C...PsP»PμCfC, PμCḥPēPSCf P·PḥPḱP©,
C...PsP»PμCfC, PμCḥPēPSCf P·PḥP'P©, C, CḥPēPiP»C-C†PμCḥPēPrC-PI) PIPēPePsPSCfPIP°P»Pē
C†PμCḥPμP· 1 PjC-CfC C†Cḥ PiC-CfP»C C PiPsC†P°C, PeCf C, PμCḥP°PiC-C—
C, PsC,, P°C†PēC, PēPSC-P±PsPj. PḥC-PrPIPēC%PμPSPSC C CḥC-PIPS-C PI
CfPiPsCfC, PμCḥC-PiP°BP»PsCfC C PI C†C-PNē C†P°CfPsPIC-PNē C, PsC†C†C- PNē
P·P°P»PēCēP°P»PsCfC C CfC, P°P±C-P»CḥPSPēPj PiC-CfP»C C C†CḥPsPiPs.

P—PjC-PSPē P»C-PiC-PrPSPsPiPs PiCḥPsC,, C-P»Cḥ PIC-Pr PIPēC...C-PrPSPsPiPs CḥC-PIPS C
PrPs P·P°PIPμCḥCēPμPSPSC C PrPsCfP»C-PrP¶PμPSPSC C (6Bḥ"24 PjC-CfC C†C-)
Cf PePsPSC, CḥPsP»CḥPsPIP°PSPēC... PeP»C-PSC-C†PSPēC... PrPsCfP»C-PrP¶PμPSPSC C... Cf
PiP°C†C-C" PSC, C-PI C-P· P Pḥ PiC-PrCfCfPjPsPIP°PSC- PSPēP¶C†Pμ.

B· PŸPμCḥPμPrPSC-PNē CḥC-PIPμPSCḤ C...PsP»PμCfC, PμCḥPēPSCf P·PḥPḱP©
P·P±C-P»CḥCēPēPICfC C PSP° 15 % Cf PiCḥCfPiC- C, PsC,, P°C†PēC, PēPSC-P±Cf 5 PjPi PrPIP°
CḥP°P·Pē PSP° PrPsP±Cf PNē PSP° 20 % Cf PiCḥCfPiC- C, PsC,, P°C†PēC, PēPSC-P±Cf 10 PjPi
PrPIP° CḥP°P·Pē PSP° PrPsP±Cf PiCḥPsC, CμPiPsPj 12 PjC-CfC C†C-PI C, PμCḥP°PiC-C—, P°
C†PμCḥPμP· 24 PjC-CfC C†C- C, PμCḥP°PiC-C— C†PμPNē CḥC-PIPμPSCḤ
P·P±C-P»CḥCēPēPICfC C PSP° 16 % Cf PiCḥCfPiC- C, PsC,, P°C†PēC, PēPSC-P±Cf 5 PjPi PrPIP°
CḥP°P·Pē PSP° PrPsP±Cf PNē PSP° 19 % Cf PiCḥCfPiC- C, PsC,, P°C†PēC, PēPSC-P±Cf 10 PjPi
PrPIP° CḥP°P·Pē PSP° PrPsP±Cf.

B· PŸPμCḥPμPrPSC-PNē CḥC-PIPμPSCḤ C...PsP»PμCfC, PμCḥPēPSCf P·PḥP'P©
P·P±C-P»CḥCēPēPICfC C PSP° 17 % Cf PiCḥCfPiC- C, PsC,, P°C†PēC, PēPSC-P±Cf 5 PjPi PrPIP°
CḥP°P·Pē PSP° PrPsP±Cf PNē PSP° 18 % Cf PiCḥCfPiC- C, PsC,, P°C†PēC, PēPSC-P±Cf 10 PjPi
PrPIP° CḥP°P·Pē PSP° PrPsP±Cf PiCḥPsC, CμPiPsPj 12 PjC-CfC C†C-PI C, PμCḥP°PiC-C—, P°
C†PμCḥPμP· 24 PjC-CfC C†C- C, PμCḥP°PiC-C— C†PμPNē CḥC-PIPμPSCḤ
P·P±C-P»CḥCēPēPICfC C PSP° 19 % Cf PiCḥCfPiC- C, PsC,, P°C†PēC, PēPSC-P±Cf 5 PjPi PrPIP°
CḥP°P·Pē PSP° PrPsP±Cf PNē PSP° 20 % Cf PiCḥCfPiC- C, PsC,, P°C†PēC, PēPSC-P±Cf 10 PjPi
PrPIP° CḥP°P·Pē PSP° PrPsP±Cf.

PḥC-CfP»C C PiCḥPēPiPēPSPμPSPSC C, PμCḥP°PiC-C— C, PsC,, P°C†PēC, PēPSC-P±PsPj
CḥC-PIPS-C P»C-PiC-PrC-PI PiPsPIPμCḥC, P°P»PēCfC C PrPs PIPēC...C-PrPSPsPiPs CḥC-PIPS C.

PŸPμCḥPμPrPSC" CfPiC-PIPIC-PrPSPsCēPμPSPSC C...PsP»PμCfC, PμCḥPēPSCf P·PḥPḱP© /

$P P_{\mu} P I P j P^{\circ} C, P s C - P r P S P \ddot{e} P N_{\circ} P^{\circ} C \bar{H} C, C \bar{H} P \ddot{e} C,$

PJ PIP_μP»PëPePsPjCř (N = 4362) PïC-CřP»CłCĤP_μC"ĆřC,ĤP°C†C-PN₂PSPsPjCř
 ĤP°PSPřPsPjC-P·PsPIP°PSPsPjCř PrPsCřP»C-PrP¶P_μPSPSC- P±P_μP·PïP_μPePë P·P° CřC†P°ĆřC,Ĥ
 PïP°C†C-C"PSC,C-PI C-P· P Ph PIC-PePsPj 50 ĤP_μPsPeC-PI C- CřC,P°ĤCĤP_μP·
 PïĤPëPSP°PN₂PjPSC- PsPrPSPëPj PrPsPrP°C,PePsPIPëPj C,,P°PeC,PsĤP_μPsPj ĤPëP·PëPeCř
 CřP_μĤC†P_μPIPs-CřCřPrPëPSPSPëC... CřCřPeP»P°PrPSP_μPSCH C†P°ĆřC,PsC,P°
 PIPëPSPëPePSP_μPSPSCł (95%-PN₂ P"Pt) PSP_μP»P_μC,P°P»ĤPSPSPiPs C-PSC,,P°ĤP_μPeC,Cř
 PjC-PsPeP°ĤPřP° PI PïP°C†C-C"PSC,C-PI, CłPeC- PsC,ĤPëPjCřPIP°P»Pë
 C,PsC,,P°C†PëC,PëPSC-P± Cř PrPsP·C- 5 PjPi PrPIP° ĤP°P·Pë PSP° PrPsP±Cř,
 C,PsC,,P°C†PëC,PëPSC-P± 10 PjPi PrPIP° ĤP°P·Pë PSP° PrPsP±Cř PN₂ C-PSPiC-P±C-C,PsĤPë
 PαPķPł, CřC,P°PSPsPIPëP»P° 0,37 (0,22; 0,57), 0,33 (0,19; 0,53) C,P° 0,16 (0,07; 0,31)
 PïP°C†C-C"PSC,P° P· PIC-PrPïPsPIC-PrPSPëPjPë CłPIPëC%P°PjPë PSP° 100 PïP°C†C-C"PSC,Ps-
 ĤP_μPsPeC-PI PIC-PrPïPsPIC-PrPSPs. P_μPsPIC-PrPsPjP»CłP»PsCřCł PïĤP_μPs PrP_μPeC-P»ĤP_μPeP°
 PIPëPïP°PrPeC-PI C-PSC,,P°ĤP_μPeC,Cř PjC-PsPeP°ĤPřP° P· P»P_μC,P°P»ĤPSPëPjPë
 PSP°CřP»C-PrPeP°PjPë, PïĤPëC†PsPjCř C†P°ĆřC,PsC,P° C-C...PSCHPsPiPs
 PIPëPSPëPePSP_μPSPSCł P±CřP»P° P°PSP°P»PsPiC-C†PSPsĤ C,P°PeC-PN₂ C†P°ĆřC,PsC,C- PI
 PïP°C†C-C"PSC,C-PI, CłPeC- PsC,ĤPëPjCřPIP°P»Pë C,PsC,,P°C†PëC,PëPSC-P±,
 C- PI PïP°C†C-C"PSC,C-PI, CłPeC- PsC,ĤPëPjCřPIP°P»Pë C-PSPiC-P±C-C,PsĤPë PαPķPł
 (PrPëPI. ĤP_μPsP·PrC-P» B«PhCřPsP±P»PëIPsCřC,C- P·P°ĆřC,PsCřCřPIP°PSPSCłB»)).
 P"PsCřP»C-PrP¶P_μPSPSCł PIPëPjP°PïP°P»Ps CřPïPsCřC,P_μĤP_μP¶P_μPSPSCł
 C%PsPSP°PN₂PjP_μPSCP_μ P·P° 1500 PïP°C†C-C"PSC,P°PjPë PïĤP_μPsC,CłPiPsPj 3 ĤP_μPsPeC-PI.

P—P»PsCłPeC-CřPSC- PSPsPIPsCžC,PIPsĤP_μPSPSCł, P·P° PIPëPSCłC,PePsPj PķPłP Pë

P P_μPIPjP°C,PsC—PrPSPëPN₂ P°ĤC,ĤPëC,

PJ PIP_μP»PëPePsPjCř (N = 4362) PïC-CřP»CłCĤP_μC"ĆřC,ĤP°C†C-PN₂PSPsPjCř
 ĤP°PSPřPsPjC-P·PsPIP°PSPsPjCř PrPsCřP»C-PrP¶P_μPSPSC- P±P_μP·PïP_μPePë P·P°
 CřC†P°ĆřC,Ĥ PïP°C†C-C"PSC,C-PI C-P· P Ph PIC-PePsPj 50 ĤP_μPsPeC-PI C- CřC,P°ĤCĤP_μP·
 PïĤPëPSP°PN₂PjPSC- PsPrPSPëPj PrPsPrP°C,PePsPIPëPj C,,P°PeC,PsĤP_μPsPj ĤPëP·PëPeCř
 CřP_μĤC†P_μPIPs-CřCřPrPëPSPSPëC... CřCřPeP»P°PrPSP_μPSCH C†P°ĆřC,PsC,P°
 PIPëPSPëPePSP_μPSPSCł (95%-PN₂ P"Pt) ĤP°P°Cř P»P_μPiP_μPSCH Cř PïP°C†C-C"PSC,C-PI,
 CłPeC- PsC,ĤPëPjCřPIP°P»Pë C,PsC,,P°C†PëC,PëPSC-P± Cř PrPsP·C- 5 PjPi PrPIP° ĤP°P·Pë
 PSP° PrPsP±Cř, C,PsC,,P°C†PëC,PëPSC-P± 10 PjPi PrPIP° ĤP°P·Pë PSP° PrPsP±Cř PN₂
 C-PSPiC-P±C-C,PsĤPë PαPķPł, CřC,P°PSPsPIPëP»P° 0,23 (0,12; 0,40), 0,32 (0,18; 0,51) C- 0,13
 (0,05; 0,26) PïP°C†C-C"PSC,P° P· PIC-PrPïPsPIC-PrPSPëPjPë CłPIPëC%P°PjPë PSP°
 100 PïP°C†C-C"PSC,Ps-ĤP_μPsPeC-PI PIC-PrPïPsPIC-PrPSPs (PrPëPI. ĤP_μPsP·PrC-P»
 B«PhCřPsP±P»PëIPsCřC,C- P·P°ĆřC,PsCřCřPIP°PSPSCłB»)). P"PsCřP»C-PrP¶P_μPSPSCł
 PIPëPjP°PïP°P»Ps CřPïPsCřC,P_μĤP_μP¶P_μPSPSCł C%PsPSP°PN₂PjP_μPSCP_μ P·P°
 1500 PïP°C†C-C"PSC,P°PjPë PïĤP_μPsC,CłPiPsPj 3 ĤP_μPsPeC-PI.

PŞP°ĆřC,PsC,P° PIPëPSPëPePSP_μPSPSCł (95%-PN₂ P"Pt) P»C-PjC,,PsPjPë PïC-Pr C†P°Ćř
 P·P°ĆřC,PsCřCřPIP°PSPSCł C,PsC,,P°C†PëC,PëPSC-P±Cř 5 PjPi PrPIP° ĤP°P·Pë PSP° PrPsP±Cř,
 C,PsC,,P°C†PëC,PëPSC-P±Cř 10 PjPi PrPIP° ĤP°P·Pë PSP° PrPsP±Cř PN₂
 C-PSPiC-P±C-C,PsĤPë-PI PαPķPł CřC,P°PSPsPIPëP»P° 0,07 (0,02; 0,18), 0,11 (0,04; 0,24) C- 0,02
 (0,00; 0,10) PïP°C†C-C"PSC,C-PI C-P· PIC-PrPïPsPIC-PrPSPëPjPë CłPIPëC%P°PjPë PSP°
 100 PïP°C†C-C"PSC,Ps-ĤP_μPsPeC-PI PIC-PrPïPsPIC-PrPSPs (PrPëPI.
 ĤP_μPsP·PrC-P» B«PhCřPsP±P»PëIPsCřC,C- P·P°ĆřC,PsCřCřPIP°PSPSCłB»)).

P_μP°C†C-C"PSC,Pë PrPëC,CłC†PsPiPs PIC-PeCř

P_μPsP»C-P°ĤC,PëPeCžP»CłĤPSPëPN₂ ĤP_μPIP_μPSC-P»ĤPSPëPN₂ C-PrC-PsPïP°C,PëC†PSPëPN₂
 P°ĤC,ĤPëC,

$P_{\mu}PsP \pm C - C \ddagger PSC - C_{\overline{H}}P_{\mu}P^{\circ}PeC \ddagger C - C - PI \ P \ddot{P}^{\circ}C \ddagger C - C''PSC, C - PI \ P \cdot P \otimes P \ddagger P_{\overline{H}}$,
 $P \cdot P^{\circ}C_{\overline{H}}P_{\mu}C''C \ddagger C, C_{\overline{H}}PsPIP^{\circ}PSC - PI \ C \dots PsPrC - PeP \gg C - PSC - C \ddagger PSPsPiPs \ PrPsC \ddagger P \gg C - PrP \ P_{\mu}PSPSC \ddagger C,$
 $C, PsC, P^{\circ}C \ddagger P \ddot{C}, P \ddot{E}PSC - P \pm C \ddagger, \ C \ddagger P \cdot PiPsPrP \ P \ C \ddagger PIP^{\circ}P \gg P \ddot{E}C \ddagger C \ddagger P \cdot P^{\circ} \ C, P \ddot{E}PiPsPj \ C -$
 $C \ddagger P^{\circ}C \ddagger C, PsC, PsC_{\overline{H}} \ PIP \ddot{E}PSP \ddot{E}PePSP_{\mu}PSPSC \ddagger P \cdot P \ddot{I}PsP \pm C - C \ddagger PSP \ddot{E}PjP \ddot{E} \ C_{\overline{H}}P_{\mu}P^{\circ}PeC \ddagger C - C \ddagger PjP \ddot{E},$
 $C \ddagger P \ddot{E}C - C \ddagger P \ddot{I}PsC \ddagger C, P_{\mu}C_{\overline{H}}C - PiP^{\circ}P \gg P \ddot{E}C \ddagger C \ddagger C \ C \ddagger \ PrPsC_{\overline{H}}PsC \ddagger P \gg P \ddot{E}C \dots \ P \ddot{I}P^{\circ}C \ddagger C - C''PSC, C - PI \ C - P \cdot$
 $P \ P_{\overline{H}}, \ P \cdot P^{\circ} \ PIP \ddot{E}PSC \ddagger C, PePsPj \ PrP_{\mu}C \ddagger P \ddot{E}C \dots \ C - PSC, P_{\mu}PeC \ddagger C - P_{\overline{N}} \ (PiC_{\overline{H}}P \ddot{E}P \ddot{I}, \ C, P^{\circ}C_{\overline{H}}P \ddot{E}PSPiC - C, C \ddagger P \ddot{E}PSC \ddagger C \ddagger P \ddot{E}C, PIC - C_{\overline{H}}C \ddagger C \ddagger PSP^{\circ} \ C - PSC, P_{\mu}PeC \ddagger C - C \ddagger C) \ C, P^{\circ} \ C_{\overline{H}}PsP \cdot P \gg P^{\circ}PrC - PI \ C - P \cdot P \pm PsPeC \ddagger$
 $C \ddagger P \gg C \ddagger PSPePsPIPs - PeP \ddot{E}C \ddagger PePsPIPsPiPs \ C, C_{\overline{H}}P^{\circ}PeC, C \ddagger \ P^{\circ}P \pm Ps \ P \cdot P^{\circ}PiP^{\circ}P \gg C_{\overline{H}}PSP \ddot{E}C \dots$
 $C_{\overline{H}}PsP \cdot P \gg P^{\circ}PrC - PI \ (P \pm C - P \gg C_{\overline{H}} \ C \ddagger \ P \ P \ddot{E}PIPsC, C -, \ PSC \ddagger PrPsC, P^{\circ}, \ P \pm P \gg C_{\overline{H}}PIP^{\circ}PSPSC \ddagger C,$
 $PiC - C_{\overline{H}}P_{\mu}PeC \ddagger C - C \ddagger C, \ PiPsP \gg PsPIPSP \ddot{E}P_{\overline{N}} \ P \pm C - P \gg C_{\overline{H}}, \ PeP^{\circ}C \ddagger P_{\mu}P \gg C_{\overline{H}}), \ C \ddagger P \ddot{E}C - C \ddagger P^{\circ}C \ddagger C, C - C \ddagger P_{\mu}$
 $PIP \ddot{E}PSP \ddot{E}PeP^{\circ}P \gg P \ddot{E} \ PI \ PrC - C, P_{\mu}P_{\overline{N}} \ P \cdot P \otimes P \ddagger P_{\overline{H}}. \ P_{\overline{H}}P \ddot{Y}P \ddagger \ P \pm C \ddagger PI \ PSP^{\circ}P_{\overline{N}}C \ddagger P^{\circ}C \ddagger C, C - C \ddagger P_{\mu}$
 $P \cdot P^{\circ}C \ddagger C, PsC \ddagger PsPIC \ddagger PIP^{\circ}PSP \ddot{E}Pj \ C \ddagger C \ddagger PiC \ddagger C, PSC - Pj \ C, C_{\overline{H}}P^{\circ}PrP \ddot{E}C \ddagger C - P_{\overline{N}}PSP \ddot{E}Pj$
 $C \ddagger P \ddot{E}PSC, P_{\mu}C, P \ddot{E}C \ddagger PSP \ddot{E}Pj \ DMARD \ (PSP^{\circ} \ 1 - P_{\overline{N}} \ PrP_{\mu}PSC_{\overline{H}} \ PrPsC \ddagger P \gg C - PrP \ P_{\mu}PSPSC \ddagger C, \ 156 \ C - P \cdot$
 $157 \ P \ddot{I}P^{\circ}C \ddagger C - C''PSC, C - PI, \ C \ddagger P \ddot{E}C - PsC, C_{\overline{H}}P \ddot{E}PjC \ddagger PIP^{\circ}P \gg P \ddot{E} \ B \ C, C_{\overline{H}}P^{\circ}PrP \ddot{E}C \ddagger C - P_{\overline{N}}PSC -$
 $C \ddagger P \ddot{E}PSC, P_{\mu}C, P \ddot{E}C \ddagger PSC - DMARD \ P \ddot{I}C_{\overline{H}}P \ddot{E}P_{\overline{N}}PjP^{\circ}P \gg P \ddot{E} \ MTX). \ P \acute{K}P^{\circ}C_{\overline{H}}P^{\circ}P \cdot C -$
 $PSP_{\mu}PrPsC \ddagger C, P^{\circ}C, PSC_{\overline{H}}Ps \ PrP^{\circ}PSP \ddot{E}C \dots \ C \% PsPrPs \ P \ddot{I}C_{\overline{H}}PsC, C - P \gg C_{\overline{H}} \ P \pm P_{\mu}P \cdot P \ddot{I}P_{\mu}PeP \ddot{E}$
 $C, PsC, P^{\circ}C \ddagger P \ddot{C}, P \ddot{E}PSC - P \pm C \ddagger \ PI \ C_{\overline{H}}P^{\circ}P \cdot C - P_{\overline{N}}PsPiPs \ P \cdot P^{\circ}C \ddagger C, PsC \ddagger C \ddagger PIP^{\circ}PSPSC \ddagger C$
 $PsPrPSPsC \ddagger P^{\circ}C \ddagger PSPs \ P \cdot P \pm C \ddagger PrC_{\overline{H}} - C \ddagger P \ddot{E}PjP \ddot{E} \ C - PSC \ddagger P \ddot{E}PjP \ddot{E} \ C, C_{\overline{H}}P^{\circ}PrP \ddot{E}C \ddagger C - P_{\overline{N}}PSP \ddot{E}PjP \ddot{E}$
 $C \ddagger P \ddot{E}PSC, P_{\mu}C, P \ddot{E}C \ddagger PSP \ddot{E}PjP \ddot{E} \ DMARD.$

$P \ddagger PSC, P_{\mu}PeC \ddagger C - C -$

$Pj \ P \ddot{I}PsPrPIC - P_{\overline{N}}PSC - P_{\overline{N}} \ C \ddagger P \gg C - PiC - P_{\overline{N}} \ C \ddagger P^{\circ}C \ddagger C, P \ddot{E}PSC - C_{\overline{H}}P_{\mu}C''C \ddagger C, C_{\overline{H}}P^{\circ}C \ddagger C - P_{\overline{N}}PSPsPiPs$
 $PrPsC \ddagger P \gg C - PrP \ P_{\mu}PSPSC \ddagger C, P^{\circ}P \cdot P \ddot{E} \ 3 \ (PrPsC \ddagger P \gg C - PrP \ P_{\mu}PSPSC \ddagger C \ JIA - I) \ C - PSC, P_{\mu}PeC \ddagger C - C -$
 $P \pm C \ddagger P \gg P \ddot{E} \ PSP^{\circ}P_{\overline{N}}C \ddagger P^{\circ}C \ddagger C, C - C \ddagger P_{\mu} \ P \ddot{I}PsPIC - PrPsPjP \gg C_{\overline{H}}PIP^{\circ}PSPsC_{\overline{H}} \ P \ddot{I}PsP \pm C - C \ddagger PSPsC_{\overline{H}}$
 $C_{\overline{H}}P_{\mu}P^{\circ}PeC \ddagger C - C''C_{\overline{H}} \ (44,3 \ %). \ P \ddagger PSC, P_{\mu}PeC \ddagger C - C - P \cdot PrP_{\mu}P \pm C - P \gg C_{\overline{H}}C \ddagger PsPiPs \ P \pm C \ddagger P \gg P \ddot{E}$
 $P \gg P_{\mu}PiPePsPiPs \ P^{\circ}P \pm Ps \ P \ddot{I}PsPjC - C_{\overline{H}}PSPsPiPs \ C \ddagger C, C \ddagger P \ddot{I}P_{\mu}PSC \ddagger C \ C, C \ddagger P \ P \ddot{E}PsC \ddagger C, C -.$

$P_{\mu}C_{\overline{H}}PsC, C \ddagger P \ddot{I}PsPj \ P \cdot PIC - C, PSPsPiPs \ P \ddot{I}P_{\mu}C_{\overline{H}}C - PsPrC \ddagger \ (PjP^{\circ}PeC \ddagger P \ddot{E}PjC \ddagger Pj \ C \ddagger P_{\mu}C_{\overline{H}}P_{\mu}P \cdot$
 $28 \ PrPSC - PI \ P \ddot{I}C - C \ddagger P \gg C \ddagger C \ P \ddot{I}C_{\overline{H}}P \ddot{E}P_{\overline{N}}PjP^{\circ}PSPSC \ddagger C \ PsC \ddagger C, P^{\circ}PSPSCHPsC - PrPsP \cdot P \ddot{E}$
 $PrPsC \ddagger P \gg C - PrP \ P \ C \ddagger PIP^{\circ}PSPsPiPs \ P \ddot{I}C_{\overline{H}}P_{\mu}P \ddot{I}P^{\circ}C_{\overline{H}}P^{\circ}C, C \ddagger) \ PI \ PsP \pm B_{\overline{H}}^{\text{TM}} \ C''PrPSP^{\circ}PSC - P_{\overline{N}}$
 $P \ddot{I}PsP \ddot{I}C \ddagger P \gg C \ddagger C \ddagger C - C - PrP \gg C \ddagger C \ PsC \ddagger C - PSPeP \ddot{E} \ P \pm P_{\mu}P \cdot P \ddot{I}P_{\mu}PeP \ddot{E} \ P \ddot{I}PsPIC - PrPsPjP \gg C \ddagger P \gg PsC \ddagger C \ddagger C$
 $P \ddot{I}C_{\overline{H}}Ps \ 7 \ P \ddot{I}P^{\circ}C \ddagger C - C''PSC, C - PI, \ C \ddagger C \ddagger P \ddot{E}C \dots \ PIP \ddot{E}PSP \ddot{E}PeP^{\circ}P \gg P \ddot{E} \ C \ddagger P_{\mu}C_{\overline{H}}P_{\overline{N}}PsP \cdot PSC -$
 $C - PSC, P_{\mu}PeC \ddagger C - C - P \ddot{I}C - Pr \ C \ddagger P^{\circ}C \ddagger C, P_{\mu}C_{\overline{H}}P^{\circ}P \ddot{I}C - C - C, PsC, P^{\circ}C \ddagger P \ddot{C}, P \ddot{E}PSC - P \pm PsPj, \ C, PsP \pm C, Ps$
 $P \ddot{I}PsPeP^{\circ}P \cdot PSP \ddot{E}Pe \ C \ddagger P^{\circ}C \ddagger C, PsC, P \ddot{E} \ C \ddagger C, P^{\circ}PSPsPIP \ddot{E}PI \ 1,92 \ P \ddot{I}P^{\circ}C \ddagger C - C''PSC, P^{\circ} \ P \cdot$
 $PIC - PrP \ddot{I}PsPIC - PrPSP \ddot{E}PjP \ddot{E} \ C \ddagger PIP \ddot{E}C \% P^{\circ}PjP \ddot{E} \ PSP^{\circ} \ 100 \ P \ddot{I}P^{\circ}C \ddagger C - C''PSC, Ps - C_{\overline{H}}PsPeC - PI. \ P''Ps$
 $C \ddagger P_{\mu}C_{\overline{H}}P_{\overline{N}}PsP \cdot PSP \ddot{E}C \dots \ C - PSC, P_{\mu}PeC \ddagger C - P_{\overline{N}} \ PSP^{\circ}P \gg P_{\mu}P \ P^{\circ}P \gg P \ddot{E} \ C, P^{\circ}PeC -: \ P \ddot{I}PSP_{\mu}PIPjPsPSC - C \ddagger C,$
 $P_{\mu}PiC - PrC \ddagger C_{\overline{H}}P^{\circ}P \gg C_{\overline{H}}PSP^{\circ} \ P_{\mu}PjPiC - C''PjP^{\circ} \ (C - P \cdot C \ddagger P \ddot{E}PSC \ddagger C \ddagger P \ddot{E}C, PsPj \ C -$
 $C \ddagger C \ddagger P \pm P \ddot{I}P_{\mu}C_{\overline{H}}C - PsC \ddagger C, P^{\circ}P \gg C_{\overline{H}}PSP \ddot{E}Pj \ P^{\circ}P \pm C \ddagger C \ddagger P_{\mu}C \ddagger PsPj), \ P \ddot{I}C - P \gg PsPSC - PrP^{\circ}P \gg C_{\overline{H}}PSP^{\circ}$
 $PeC - C \ddagger C, P^{\circ}, \ P^{\circ}P \ddot{I}P_{\mu}PSP \ddot{E}P \ddot{E}C \ddagger P \ddot{E}C,; \ P \ddot{I}C - C''P \gg PsPSP_{\mu}C, C_{\overline{H}}P \ddot{E}C, C \ddagger P \ddot{I}C_{\overline{H}}P \ddot{E}C \ddagger P \ddot{E}PSP_{\mu}PSP \ddot{E}P_{\overline{N}}$
 $P_{\mu}C \ddagger P_{\mu}C_{\overline{H}}P \ddot{E}C \dots \ C - C \ddagger PjP \ddot{E}; \ P^{\circ}P \pm C \ddagger C \ddagger P_{\mu}C \ddagger PeC - PSC \ddagger C - PIPeP \ddot{E} \ C, P^{\circ} \ C - PSC, P_{\mu}PeC \ddagger C - C -$
 $C \ddagger P_{\mu}C \ddagger PsPIP \ddot{E}PIC - PrPSP \ddot{E}C \dots \ C \ddagger P \gg C \ddagger C \dots \ C - PI.$

$P' \ PsP \pm B_{\overline{H}}^{\text{TM}} \ C''PrPSP^{\circ}PSC - P_{\overline{N}} \ P \ddot{I}PsP \ddot{I}C \ddagger P \gg C \ddagger C \ddagger C - C - PrP \gg C \ddagger C \ PsC \ddagger C - PSPeP \ddot{E} \ P \pm P_{\mu}P \cdot P \ddot{I}P_{\mu}PeP \ddot{E}$
 $3 \ P \ddot{I}P^{\circ}C \ddagger C - C''PSC, P \ddot{E} \ PjP^{\circ}P \gg P \ddot{E} \ PSP_{\mu}C \ddagger P_{\mu}C_{\overline{H}}P_{\overline{N}}PsP \cdot PSC - C - PSC, P_{\mu}PeC \ddagger C - C -$
 $PsP \ddot{I}P_{\mu}C_{\overline{H}}C - P \cdot C \ddagger C_{\overline{H}}C \ddagger PsPiPs \ P \ddot{I}P_{\mu}C_{\overline{H}}P \ddot{I}P_{\mu}C \ddagger C \ddagger C \ PI \ PjP_{\mu}P \ P^{\circ}C \dots \ PIC - PePSP^{\circ} \ P \cdot PIC - C, PSPsC \ddagger C, C -,$
 $C, PsP \pm C, Ps \ C \ddagger P^{\circ}C \ddagger C, PsC, P^{\circ} \ PIP \ddot{E}PSP \ddot{E}PePSP_{\mu}PSPSC \ddagger C \ddagger P \ddot{E}C \dots \ C \ddagger PIP \ddot{E}C \% \ C \ddagger C, P^{\circ}PSPsPIP \ddot{E}P \gg P^{\circ}$
 $0,82 \ P \ddot{I}P^{\circ}C \ddagger C - C''PSC, P^{\circ} \ P \cdot PIC - PrP \ddot{I}PsPIC - PrPSP \ddot{E}PjP \ddot{E} \ C \ddagger PIP \ddot{E}C \% P^{\circ}PjP \ddot{E} \ PSP^{\circ}$
 $100 \ P \ddot{I}P^{\circ}C \ddagger C - C''PSC, Ps - C_{\overline{H}}PsPeC - PI. \ P \otimes P_{\mu} \ PI \ PsPrPSPsPiPs \ (1) \ PrPsPrP^{\circ}C, PePsPIPsPiPs$
 $P \ddot{I}P^{\circ}C \ddagger C - C''PSC, P^{\circ} \ PIP \ddot{E}PSP \ddot{E}PeP \gg P^{\circ} \ C \ddagger P_{\mu}C_{\overline{H}}P_{\overline{N}}PsP \cdot PSP^{\circ} \ C - PSC, P_{\mu}PeC \ddagger C - C \ddagger C$
 $PsP \ddot{I}P_{\mu}C_{\overline{H}}C - P \cdot C \ddagger C_{\overline{H}}C \ddagger PsPiPs \ P \ddot{I}P_{\mu}C_{\overline{H}}P \ddot{I}P_{\mu}C \ddagger C \ddagger C \ P \ddot{I}PsP \cdot P^{\circ} \ PjP_{\mu}P \ P^{\circ}PjP \ddot{E} \ PIC - PePSP^{\circ}$
 $P \cdot PIC - C, PSPsC \ddagger C, C -.$

P PsP·P»P°PrPë P· P±PsPeCé PiPµC‡C-PSPePë

P' CḡPµC"ĆĲ,CḡP°C†C-PNēPSPsPjCṛ PrPsCĲP»C-PrP¶PµPSPSC- P· PIPëPIC‡PµPSPSCĲ
PĲPsPeP°P·P°PSPSCĲ P®P†Pḡ PrPs CṛC‡P°ĆĲ,C- PrPsPĲCṛCĲPeP°P»PëCĲCĲ P»PëC€Pµ
PĲP°C†C-C"psc,Pë, Cṛ CĲPePëC... CḡC-PIPSC- PḡPŸPŸ C- PḡP>PŸ PĲPµCḡPµPIPëC%oCṛPIP°P»Pë
PIPµCḡC...PSCḡ PjPµP¶Cṛ PSPsCḡPjPë PjPµPSC€ PSC-P¶ Cṛ 1,5 CḡP°P·Pë.
P' PsP±Bḡ™C"PrPSP°PSC-PNē PĲPsPĲCṛP»CĲC†C-C— PrP»CĲ PsC†C-PSPePë P±PµP·PĲPµPePë
P±CṛP»Ps 2 PĲP°C†C-C"psc,Pë, Cṛ CĲPePëC... CĲPĲPsCĲC,PµCḡC-PiP°P»PsCĲCĲ
PĲC-PrPIPëC%oPµPSPSCĲ CḡC-PIPSCĲ PḡP>PŸ ≥ 3 × P'PḡPḡ PĲC-Pr C‡P°CĲ
2 PĲPsCĲP»C-PrPsPIPSPëC... PIC-P·PëC,C-PI. P-PsPrPSPµ C-P· C†PëC... CĲPIPëC%o
PSPµ PIC-PrPĲPsPIC-PrP°P»Ps PeCḡPëC,PµCḡC-CĲPj P·P°PePsPSCṛ PĲP°CĲ. PḡP±PëPrPIP°
PĲP°C†C-C"psc,Pë PsC,CḡPëPjCṛPIP°P»Pë CĲCṛPĲCṛC,PSCḡ C,PµCḡP°PĲC-Cḡ PḡPŸPĲ, C-
PePsP¶PSPµ C-P· C†PëC... CĲPIPëC%o P·PSPëPeP»Ps PĲC-CĲP»CĲ PĲCḡPëPĲPëPSPµPSPSCĲ
P·P°CĲC,PsCĲCṛPIP°PSPSCĲ PḡPŸPĲ PNē PsCĲC,P°C,PsC‡PSPsPiPs PĲCḡPëPĲPëPSPµPSPSCĲ
C,PµCḡP°PĲC-C— C,PsC,,P°C†PëC,PëPSC-P±PsPj.

P>P°P±PsCḡP°C,PsCḡPSC- P°PSP°P»C-P·Pë

P—PjC-PSPë PI CḡPµP·CṛP»CḡC,P°C,P°C... P»P°P±PsCḡP°C,PsCḡPSPëC... P°PSP°P»C-P·C-PI Cṛ
PĲP°C†C-C"psc,C-PI P· P®P†Pḡ, P·P°CḡPµC"ĆĲ,CḡPsPIP°PSC- PI PĲCḡPsPĲCḡP°PjC-
PeP»C-PSC-C‡PSPëC... PrPsCĲP»C-PrP¶PµPSCḡ, CṛP·PiPsPrP¶CṛPIP°P»PëCĲCĲ P·C-
P·PjC-PSP°PjPë, CĲPeC- CĲPĲPsCĲC,PµCḡC-PiP°P»PëCĲCḡ Cṛ PrPsCḡPsCĲP»PëC...
PĲP°C†C-C"psc,C-PI C-P· P Pḡ. P' CḡPµC"ĆĲ,CḡP°C†C-PNēPSPsPjCṛ PrPsCĲP»C-PrP¶PµPSPSC-
P· PIPëPIC‡PµPSPSCĲ PĲPsPeP°P·P°PSPSCĲ P®P†Pḡ PrPs CṛC‡P°ĆĲ,C-
PrPsPĲCṛCĲPeP°P»PëCĲCĲ P»PëC€Pµ PĲP°C†C-C"psc,Pë P· PeC-P»CḡPeC-CĲC,Cḡ
C,CḡPsPjP±PsC†PëC,C-PI ≥ 100 000 PeP»C-C,PëPS/PjPj³, C,PsPjCṛ PSP°CḡP°P·C- PSPµPjP°C"
PrPsCĲC,CṛPĲPSPs— C-PSC,,PsCḡPjP°C†C-C— C%oPsPrPs P»C-PeCṛPIP°PSPSCĲ
PĲP°C†C-C"psc,C-PI P· P®P†Pḡ, Cṛ CĲPePëC... PrPs PĲPsC‡P°C,PeCṛ C,PµCḡP°PĲC-C—
C,PsC,,P°C†PëC,PëPSC-P±PsPj PeC-P»CḡPeC-CĲC,Cḡ C,CḡPsPjP±PsC†PëC,C-PI
CĲC,P°PSPsPIPëC,Cḡ < 100 000 PeP»C-C,PëPS/PjPj³.

PµPsPIC-PrPsPjP»PµPSPSCĲ PĲCḡPs PĲC-PrPsP·CḡCḡPIP°PSC- PĲPsP±C-C‡PSC-
CḡPµP°PeC†C-C—

PµPsPIC-PrPsPjP»PµPSPSCĲ PĲCḡPs PĲC-PrPsP·CḡCḡPIP°PSC- PĲPsP±C-C‡PSC-
CḡPµP°PeC†C-C— PĲC-CĲP»CĲ CḡPµC"ĆĲ,CḡP°C†C-C— P»C-PeP°CḡCĲCḡPePsPiPs
P·P°CĲPsP±Cṛ PjP°C" PIP°P¶P»PëPIPµ P·PSP°C‡PµPSPSCĲ. PĲPµ PrP°C" P·PjPsPĲCṛ
PĲCḡPsPiPsPrPëC,Pë PjPsPSC-C,PsCḡPëPSPi CĲPĲC-PIPIC-PrPSPsC€PµPSPSCĲ
PePsCḡPëCĲC,Cḡ/CḡPëP·PëPe PĲCḡPë P·P°CĲC,PsCĲCṛPIP°PSPSC- C†CḡPsPiPs
P»C-PeP°CḡCĲCḡPePsPiPs P·P°CĲPsP±Cṛ. PḡPµPrPëC‡PSPëPj C,P°
C,,P°CḡPjP°C†PµPIC,PëC‡PSPëPj PĲCḡP°C†C-PIPSPëPeP°Pj, P° C,P°PePsP¶ PĲP°C†C-C"psc,P°Pj
P°P±Ps C—C... P·P°PePsPSPSPëPj PĲCḡPµPrCĲC,P°PIPSPëPeP°Pj CĲP»C-Pr
PĲPsPIC-PrPsPjP»CĲC,Pë PĲCḡPs CṛCĲC- PIPëPĲP°PrPePë PĲC-PrPsP·CḡCḡPIP°PSPëC...
PĲPsP±C-C‡PSPëC... CḡPµP°PeC†C-PNē C,P° PIC-PrCĲCṛC,PSPsCĲC,C-
PµC,,PµPeC,PëPIPSPsCĲC,C- P»C-PeP°CḡCĲCḡPePsPiPs P·P°CĲPsP±Cṛ C‡PµCḡPµP·
P°PIC,PsPjP°C,PëP·PsPIP°PSCṛ C-PSC,,PsCḡPjP°C†C-PNēPSCṛ CĲPëCĲC,PµPjCṛ P·
C,,P°CḡPjP°PePsPSP°PiP»CĲPrCṛ P·P° PĲPsCĲPëP»P°PSPSCĲPj: <https://aisf.dec.gov.ua>.

PŸPµCḡPjC-PS PĲCḡPëPrP°C,PSPsCĲC,C-. 3 CḡPsPePë.

PJPjPsPIPe P·P±PμCηC-PiP°PSPSCII.

P—P±PμCηC-PiP°C,Pë PïCηPë C,PμPjPïPμCηP°C,CíCηC- PSPëP¶C‡Pμ 30 B°PŸ.

PJPïP°PePsPIPeP°.

PŸP°P±P»PμC,PePë, PIPeCηPëC,C- PïP»C-PIPePsPIPsCη PsP±PsP»PsPSPePsCη, PïPs 5 PjPi, B„- 14: PeP°CηC,PsPSPSP° PePsCηPsP±PeP°, C%oPs PjC-CíC,PëC,CH 1 P±P»C-CíC,PμCη; PïPs 14 C,P°P±P»PμC,PsPe Cí P±P»C-CíC,PμCηC-;

C,P°P±P»PμC,PePë, PIPeCηPëC,C- PïP»C-PIPePsPIPsCη PsP±PsP»PsPSPePsCη, PïPs 5 PjPi, B„- 56: PeP°CηC,PsPSPSP° PePsCηPsP±PeP°, C%oPs PjC-CíC,PëC,CH 4 P±P»C-CíC,PμCηPë; PïPs 14 C,P°P±P»PμC,PsPe Cí P±P»C-CíC,PμCηC-.

PъP°C,PμPiPsCηC-CII PIC-PrPïCíCíPeCí. P—P° CηPμC‡PμPïC,PsPj.

P'PëCηPsP±PSPëPe.

P¶C„P°PNëP·PμCη PъPμPSCηC„PμPeC‡CíCηPëPSPi P”PsPNëC‡P»PμPSPr P”PjP±PΓ / Pfizer Manufacturing Deutschland GmbH.

PъC-CíC‡PμP·PSP°C...PsPrP¶PμPSPSCII PIPëCηPsP±PSPëPeP° C,P° PNëPsPiPs P°PrCηPμCíP° PjC-CíC‡CII PïCηPsPIP°PrP¶PμPSPSCII PrC-CIIP»CHPSPsCíC,C-.

PъCíCíPIP°P»CHPrP°P»CH 1, 79108 PαCηP°PNëP±CíCηPi P‡Pj P'CηP°PNëCíPïP°Cí, PќC-PjPμC‡C‡PëPSP° / Mooswaldallee 1, 79108 Freiburg Im Breisgau, Germany.