

Р+РќРŸРŸР РЈРЉР+Р+РІ

РrP»CЦ РjPμPrPөC±PSPsPiPs P·P°CГC,PsCГCfPIP°PSPSCЦ P»C-PөP°CГCГCНPөPsPiPs P·P°CГC±CГ

РŸРђP'P+PŸ

(SAWIS)

РŸРөP»P°Pr:

PrC-CHC±P° CГPμC±PsPIPөPSP°: PrC-C''PSPsPiPμCГC,;

1 C,P°P±P»PμC,PөP° PjC-CГC,PөC,CH PrC-C''PSPsPiPμCГC,CГ 2 PjPi;

PrPsPiPsPjC-PПPSC- CГPμC±PsPIPөPSPө: PjP°PiPSC-CH CГC,PμP°CГP°C,, C,P°P»CHPө, PөCГPsCГPiPsPIC-PrPsPS (C,PөPi Pђ), PiPsPIC-PrPsPS РЉ-25, C†PμP»CГP»PsP·P° PjC-PөCГPsPөCГPөCГC,P°P»C-C±PSP°, PөCГPsC...PjP°P»CH PөCГPөCГCГP†P·CЦPSPөP№ PiCГPμPПPμP»P°C,PөPSC-P·PsPIP°PSPөP№, P»P°PөC,PсP·Pө PjPsPSPsPiC-PrCГP°C,.

P»C-PөP°CГCГCНPөP° C,,PsCГPjP°. PŸP°P±P»PμC,PөPө.

PкCГPSPsPIPSC- C,,C-P·PөPөPs-C...C-PjC-C±PSC- PIP»P°CГC,PөPIPsCГC,C-: P±C-P»PsPiPs P°P±Ps PjP°P№PПPμ P±C-P»PsPiPs PөPsP»CHPsCГCГ, PөCГCГPiP»C-, PiP»P°CГPөC- C,P°P±P»PμC,PөPө, P· C,,P°CГPөPsCГ C- PiCГP°PIC-CГPIP°PSPSCЦPj B«✗» P· PsPrPSPsPiPs P±PsPөCГ,B B«RGB» - P· C-PSCөPsPiPs. P''C-P°PjPμC,CГ 7 PjPj.

РќP°CГPjP°PөPsC,PμCГP°PiPμPIC,PөC±PSP° PiCГCГPiP°. P''PsCГPjPsPSPө CГC,P°C,PμPIPөC... P·P°P»PsP· C,P° PiCГPμPiP°CГP°C,Pө, CЦPөC- P·P°CГC,PsCГPsPICГCГC,CH PiCГPө PiP°C,PsP»PsPiC-C— CГC,P°C,PμPIPөC... PsCГPiP°PSC-PI. PμCГPsPiPμCГC,PsPiPμPSPө. РЉPsPr PђPŸPГ G03D B08.

РќP°CГPjP°PөPsP»PsPiC-C±PSC- PIP»P°CГC,PөPIPsCГC,C-.

РќP°CГPjP°PөPsPrPөPSP°PjC-PөP°.

P''C-C''PSPsPiPμCГC, вђ" PiPsC...C-PrPSPμ PSPsCГC,PμCГC,PsCГC,PμCГPsPSCГ P±PμP· P°PSP†CГPsPiPμPSPSPsC— C,P° P· PiPμPIPSPsCГ P°PSC,PөP°PSP†CГPsPiPμPSPSPsCГ P°PөC,PөPIPSC-CГC,CГ, C%өPs CГC,P°PSPsPIPөC,CH PiCГPөP±P»PөP·PSPs PsPrPSCГ C,CГPμC,PөPSCГ P°PөC,PөPIPSPsCГC,C- C†PөPiCГPsC,PμCГPsPSCГ P°C†PμC,P°C,CГ. P''C-C''PSPsPiPμCГC, P·Piвђ™ CЦP·CГC''C,CHCГCЦ P· CГPμC†PμPiC,PsCГP°PjPө PiCГPsPiPμCГC,PμCГPsPSCГ CГ PjP°C,C†C- C,C-P»CHPөPө P· 10 % PIC-PrPSPsCГPSPsCГ P°C,,C-PSPSC-CГC,CГ. PќPμP·PIP°PПP°CГC±Pө PSP° PSPөP·CHPөCГ P°C,,C-PSPSC-CГC,CH PrPs CГPμC†PμPiC,PsCГC-PI PiCГPsPiPμCГC,PμCГPsPSCГ, PrC-C''PSPsPiPμCГC, PIPөCЦPIP»CЦC'' CГPөP»CHPSPөP№ PiCГPsPiPμCГC,PsPiPμPSPSPөP№ PμC,,PμPөC, *in vivo*. P''C-C''PSPsPiPμCГC, PSPμ PiCГPsCЦPIP»CЦC'' P·PSP°C±PSCГ P°PSP†CГPsPiPμPSPSCГ, PjC-PSPμCГP°P»PsPөPsCГC,PөPөPsC—PrPSCГ P°P±Ps PiP»CHPөPsPөPsCГC,PөPөPsC—PrPSCГ

P°PeC, PëPIPSC-CÍC, CH *in vivo*.

P°C-C°PSPsPiPµCÍC, PIPiP»PëPIP°C° PSP° PµPSPPrPsPjPµC, CĤC-PsP., P·PjPµPSC€CfCĤC±Pë PµPSPPrPsPiPµPSPSCr PíCĤPsPrCfPeC†C-CĤ PµCÍC, CĤP°PrC-PsP»Cf C- C, P°PePëPj C±PëPSPsPj PíCĤPëPiPSC-C±CfCĤC±Pë C, CĤPsC,, C-C±PSC- PµC,, PµPeC, Pë PµCÍC, CĤP°PrC-PsP»Cf PSP° PµCfC, PsPiC-C±PSPëPNë C, P° PµPeC, PsPiC-C±PSPëPNë PµPSPPrPsPjPµC, CĤC-PNë. PµCĤPë P±PµP·PiPµCĤPµCĤPIPSPsPjCf P·P°CÍC, PsCÍCfPíP°PSPSC- PrC-C°PSPsPiPµCÍC, PíCĤPëP·PIPsPrPëC, CH PrPs CÍC, PIPsCĤPµPSPSCÍ PíC-PíPsPµCÍC, CĤPsPiPµPSPSPsPiPs, PíC-PíPµCĤPiPµCÍC, P°PiPµPSPSPsPiPs PµPSPPrPsPeCĤPëPSPSPsPiPs CÍPµCĤPµPrPsPIPëC%P°, C%Ps CÍPíCĤPëC±PëPSCÍC° PíPsC±P°C, PePsPICr PrPµC†PëPrCfP°P»C-P·P°C†C-CĤ C, PeP°PSPëPSPë PµPSPPrPsPjPµC, CĤC-CÍ P· PíPsPrP°P»CHC€PsCĤ P°C, CĤPsC,, C-C°CĤ PµPSPPrPsPjPµC, CĤC-PsC-PrPSPëC... PIPsPiPSPëC%.

P°PSC- C%PsPrPs PµC,, PµPeC, PëPIPSPsCÍC, C-

Pj PíCĤPsC†PµCÍC- C, CĤPëPjC-CÍCÍC±PSPsPiPs PrPsCÍP»C-PrP¶PµPSPSCÍ P· CfC±P°CÍC, CĤ 198 PíP°C†C-C°PSC, PsPe P· PµPSPPrPsPjPµC, CĤC-PsP·PsPjB P±CfP»Ps PíPsPeP°P·P°PSPs PíPµCĤPµPIP°PíCf PrC-C°PSPsPiPµCÍC, Cí 2 PjPi PíPµCĤPµPr PíP»P°C†PµP±Ps. P°C-P»CH Cí PrC-P»CÍPSC†C- C, P°P·P°, PíPsPIBĤ™ CÍP·P°PSPëPNë P· PµPSPPrPsPjPµC, CĤC-PsP·PsPj, PIPëPjC-CĤCĤPIP°P»Pë P·P° PrPsPíPsPjPsPiPsCĤ PIC-P·CfP°P»CHPSPsC- P°PSP°P»PsPiPsIPsC- C€PeP°P»Pë (0-100 PjPj). PŞPµCĤPµP· 3 PjC-CÍCÍC†C- C, PµCĤP°PíC-C- P±CfP»P° PIPëP·PSP°C±PµPSP° CÍC, P°C, PëCÍC, PëC±PSPs P·PSP°C±CfC%P° CĤC-P·PSPëC†CÍ PíPsCĤC-PIPSCÍPSPs P· PíP»P°C†PµP±Ps (D = 12,3 PjPj; 95 % P°Pt: 6,4 BĤ° 18,1; p<0,0001) C, P° PeP»C-PSC-C±PSPs P·PSP°C±CfC%Pµ P·PjPµPSC€PµPSPSCÍ P±PsP»CĤ PíPsCĤC-PIPSCÍPSPs P· PíPsC±P°C, PePsPIPëPj CĤC-PIPSPµPj (CÍPµCĤPµPrPSC° P·PjPµPSC€PµPSPSCÍ = 27,4 PjPj B± 22,9).

PŞPµCĤPµP· 3 PjC-CÍCÍC†C- P»C-PeCfPIP°PSPSCÍ P·PjPµPSC€PµPSPSCÍ P±PsP»CĤ Cí PrC-P»CÍPSC†C- PjP°P»PsPiPs C, P°P·P°, C%Ps P±CfPI PíPsPIBĤ™ CÍP·P°PSPëPNë P· PµPSPPrPsPjPµC, CĤC-PsP·PsPj, PSP° 50 % P°P±Ps P±C-P»CHC€Pµ P±CfP»Ps PrPsCÍCÍPíPSCfC, Ps Cí 37,3 % PíP°C†C-C°PSC, PsPe, CÍPeC- PsC, CĤPëPjCfPIP°P»Pë PrC-C°PSPsPiPµCÍC,, C, P°P±P»PµC, PePë 2 PjPi (PíP»P°C†PµP±Ps: 19,8 %) P±PµP· PIC-PrPíPsPIC-PrPSPsPiPs P·P±C-P»CHC€PµPSPSCÍ PrPsP·Pë CÍCfPíCfC, PSCĤPsPiPs P·PSPµP±PsP»CĤPIP°P»CHPSPsPiPs P·P°CÍPsP±Cf; P·PjPµPSC€PµPSPSCÍ P±PsP»CĤ Cí PrC-P»CÍPSC†C- PjP°P»PsPiPs C, P°P·P°, PíPsPIBĤ™ CÍP·P°PSPsPiPs P· PµPSPPrPsPjPµC, CĤC-PsP·PsPj, PSP° 75 % P°P±Ps P±C-P»CHC€Pµ (C, P°PePsP¶ P±PµP· PIC-PrPíPsPIC-PrPSPsPiPs P·P±C-P»CHC€PµPSPSCÍ PrPsP·Pë CÍCfPíCfC, PSCĤPsPiPs P·PSPµP±PsP»CĤPIP°P»CHPSPsPiPs) P±CfP»Ps PrPsCÍCÍPíPSCfC, Ps Cí 18,6 % PíP°C†C-C°PSC, PsPe, CÍPeC- PsC, CĤPëPjCfPIP°P»Pë PrC-C°PSPsPiPµCÍC,, C, P°P±P»PµC, PePë 2 PjPi (PíP»P°C†PµP±Ps: 7,3 %).

P°C-PrPeCĤPëC, Pµ PíCĤPsPrPsPIP¶PµPSPSCÍ C†CHPsPiPs PíP»P°C†PµP±Ps- PePsPSC, CĤPsP»CHPsPIP°PSPsPiPs PrPsCÍP»C-PrP¶PµPSPSCÍ PíPsPeP°P·P°P»Ps P±PµP·PiPµCĤPµCĤPIPSPµ P·PjPµPSC€PµPSPSCÍ PíPsPIBĤ™ CÍP·P°PSPsPiPs P· PµPSPPrPsPjPµC, CĤC-PsP·PsPj P±PsP»CĤ PI PrC-P»CÍPSC†C- C, P°P·P° PíCĤPë P»C-PeCfPIP°PSPSC- C, CĤPëPIP°P»C-CÍC, CĤ PrPs 15 PjC-CÍCÍC†C-PI.

P PµP·CfP»CHC, P°C, Pë PíP»P°C†PµP±Ps-PePsPSC, CĤPsP»CHPsPIP°PSPëC... PrPsCÍP»C-PrP¶PµPSCĤ PíC-PrC, PIPµCĤPµPrP¶CfPIP°P»PëCÍCÍ CĤPµP·CfP»CHC, P°C, P°PjPë, PsC, CĤPëPjP°PSPëPjPë Cí PíCĤPsC†PµCÍC- C€PµCÍC, PëPjC-CÍCÍC±PSPsPiPs P°PeC, PëPIPSPs PePsPSC, CĤPsP»CHPsPIP°PSPsPiPs PrPsCÍP»C-PrP¶PµPSPSCÍ PíPsCĤC-PIPSCÍPSPs P· P°PiPsPSC-CÍC, PsPj PíPsPSP°PrPsC, CĤPsPíC-PS-CĤPëP»C-P·PëPSPi PíPsCĤPjPsPSCf P·

CfC#P°CfC, C# 252 PiP°C+C-C" PSC, PsPe P· PµPSPPrPsPjPµC, C#C-PsP·PsPj.

P#C#P# PrPsCfP»C-PrP¶PµPSPSC¶ P· CfC#P°CfC, C# 252 PiP°C+C-C" PSC, PsPe, C¶PeC-
PsC, C#P#PjCfPIP°P»P# PrC-C" PSpSiPµCfC, PiPs 2 PjPi PSP° PrPsP±Cf,
PiC#PsPrPµPjPsPSCfC, C#CfPIP°P»P# C-CfC, PsC, PSPµ P·PSP#P¶PµPSPSC¶
PµPSPPrPsPjPµC, C#C-PsC-PrPSP#C... CfC#P°P¶PµPSC# C#PµC#PµP· 6 PjC-CfC¶C+C-PI
P»C-PeCfPIP°PSPSC¶.

PJ PiC#PsC+PµCfC- PSPµPIPµP»P#PePsPiPs PrPsCfP»C-PrP¶PµPSPSC¶ (n=8 PSP° PiC#CfPiCf
PrPsP·CfPIP°PSPSC¶) P·P°CfC, PsCfCfPIP°PSPSC¶ PrC-C" PSpSiPµCfC, Cf PI PrPsP·C- 1 PjPi
PSP° PrPsP±Cf PIP#C¶PIP#P»Ps PIC-PrCfCfC, PSC-CfC, C# PsPICfP»C¶C+C-C- C#PµC#PµP· 1
PjC-CfC¶C+C# C, PµC#P°PiC-C-. P"C-C" PSpSiPµCfC, PSPµ PrPsCfP»C-PrP¶CfPIP°P»P#
C%°PsPrPs PePsPSC, C#P°C+PµPiC, P#PIPSPsC- PµC,, PµPeC, P#PIPSPsCfC, C- Cf
P±C-P»C#C#P#C... PrPsCfP»C-PrP¶PµPSPSC¶C....

P"°PSC- C%°PsPrPs P±PµP·PiPµPeP#

P C-PIPµPSC# PµPSPPrPsPiPµPSPSPsPiPs PµCfC, C#PsPiPµPSCf C, C-P»C#PeP# PiPsPjC-C#PSPs
PiC#P#PiPSC-C#CfC" C, C#CfC¶ PiC-Pr C#P°Cf P»C-PeCfPIP°PSPSC¶ PrC-C" PSpSiPµCfC, PsPj,
C, P°P±P»PµC, PeP°PjP# 2 PjPi.

P"PsC, PµPiPµC# C#PµP·CfP»C#C, P°C, P# PrPsPiPiPsCfC, C#PsPePsPIP#C...
PrPsCfP»C-PrP¶PµPSC# PjC-PSPµC#P°P»C#PSPsC- C%°C-P»C#PSPsCfC, C- PeC-CfC, PsPe
(P#P#P#) C- C#P#P#P#PeCf PiPµC#PµP»PsPjC-PI Cf PiP°C+C-C" PSC, PsPe, C¶PeC-
P·P°CfC, PsCfPsPICfC#C, C# PrC-C" PSpSiPµCfC,, C, P°P±P»PµC, PeP# 2 PjPi, PiPsPeP# C%°Ps
PSPµPrPsCfC, CfPiPSC-. P#P#P# PsC+C-PSC#PIP°P»P# Cf 21 PrPsC#PSCfP»PsC-
PiP°C+C-C" PSC, PeP# PrPs C, P° PiC-CfP»C¶ 6 PjC-CfC¶C+C-PI P»C-PeCfPIP°PSPSC¶
PrC-C" PSpSiPµCfC, PsPj, C, P°P±P»PµC, PeP°PjP# 2 PjPi. P-PSP#P¶PµPSPSC¶
CfPµC#PµPrPSC#PsPiPs PiPsPeP°P·PSP#PeP° P#P#P# PIP#C¶PIP»PµPSPs PSPµ P±CfP»Ps. PJ
29 PiP°C+C-C" PSC, PsPe, C¶PeC- PsC, C#P#PjCfPIP°P»P# P»PµP#PiC#PsC#PµP»C-PSCf
P°C+PµC, P°C,, CfPµC#PµPrPSC" P·PSP#P¶PµPSPSC¶ 4,04 % B± 4,84 P±CfP»Ps
PIC-PrP·PSP°C#PµPSPs P·P° C, PsP# P¶Pµ PiPµC#C-PsPr (D PjC-P¶ PiC#CfPiP°PjP# = 4,29 %, 95
% P"Pt: 1,93-6,66, C# <0,0003).

P#Pµ CfPiPsCfC, PµC#C-PiP°P»PsCfC¶ P·PSP°C#PSPsPiPs PIPiP»P#PICf PSP°
CfC, P°PSPPrP°C#C, PSC- P»P°P±PsC#P°C, PsC#PSC- PiPsPeP°P·PSP#PeP#, Cf C, PsPjCf
C#P#CfP»C- PSP° C#PµP·CfP»C#C, P°C, P# P°PSP°P»C-P·Cf PeC#PsPIC-,
P±C-PsC...C-PjC-C#PSPsPiPs P°PSP°P»C-P·Cf PeC#PsPIC-, C#C-PIPµPSC#
PiPµC#C-PSPePsPIP#C... C,, PµC#PjPµPSC, C-PI, C#C-PIPµPSC# P»C-PiC-PrC-PI C- HbA1P#,
PiC-Pr C#P°Cf P»C-PeCfPIP°PSPSC¶ PrC-C" PSpSiPµCfC, PsPj, C, P°P±P»PµC, PeP°PjP# 2 PjPi,
CfPiC#PsPrPsPIP¶ 15 PjC-CfC¶C+C-PI (N = 168).

P"°PSC- C%°PsPrPs P±PµP·PiPµPeP# PrP»C¶ PiC-PrP»C-C, PeC-PI

P·PµP·PiPµPeCf PrC-C" PSpSiPµCfC, Cf, C, P°P±P»PµC, PsPe 2 PjPi, C%°PsPrPs P#P#P# P±CfP»Ps
PrPsCfP»C-PrP¶PµPSPs Cf PiC#PsC+PµCfC- PSPµPePsPSC, C#PsP»C#PsPIP°PSPsPiPs
PrPsCfP»C-PrP¶PµPSPSC¶ PiC#PsC, C¶PiPsPj 12 PjC-CfC¶C+C-PI P·P° CfC#P°CfC, C- 111
PiP°C+C-C" PSC, PsPe PiC-PrP»C-C, PePsPiPsPiPs PIC-PeCf (PIC-PePsPj PIC-Pr 12 PrPs <18
C#PsPeC-PI) P·PeP»C-PSC-C#PSPs PiC-PrPsP·C#C#PIP°PSP#Pj P°P±Ps
PiC-PrC, PIPµC#PµPrP¶PµPSP#Pj PµPSPPrPsPjPµC, C#C-PsP·PsPj. P#PµC#PµPrPSC¶
PIC-PrPSPsCfPSP° P·PjC-PSP° P#P#P# PiPsPiPµC#PµPePsPiPsPiPs PIC-PrPrC-P»Cf
C...C#PµP±C, P° (L2 B# L4) PIC-Pr PIP#C...C-PrPSP#C... PiPsPeP°P·PSP#PeC-PI Cf 103

РiР°С†С-С"РSC,PsPe С-Р· РiРëРjС-СҫСҫРiР°РSPSCПj РҫР°Рљ СҫС,Р°РSPsРiРëР»Р° -1,2 %.
РµРsРiС,PsСҫРSPµ РiРëРjС-СҫСҫРiР°РSPSCП СҫРµСҫРµРµ· 6 РjС-СҫСҫС†С-Рi РiС-СҫР»Сҫ
Р·Р°РеС-РSCҫРµРSPSCП Р»С-РeСҫРiР°РSPSCП Сҫ СҫСҫР±РiСҫСҫРiС- Р·С- Р·РSPëРµРµРµРjРё
Р·РSP°СҫРµРµРSPSCПjРё РҫР°Рљ РiРsРeР°Р°·Р°Р»Рs РiС-РrРiРëС°РµРµРSPSCП РҫР°Рљ РrРs вҫ

Р"Р°РSC- Р· Р±РµР·РiРµРµРё РiСҫРё РrРsРiРiРsС,СҫРёРiР°Р»Р»РsРjСҫ Р·Р°СҫС,PsСҫСҫРiР°РSPSC-

Р'СҫР»Рs РiСҫРsРiРµРµРµРµРµ РsР±СҫРµСҫРiР°Р»Р»Р°Р-РµРSPµ
РiС-СҫР»СҫСҫРµРµС"СҫС,СҫР°Сҫ-РµРSPµ РrРsСҫР»С-РrРµРµРµРSPSCП Р· Р°РeС,РёРiРSPëРj
СҫРiРsСҫС,РµСҫРµРµРµРµРSPSCП Р· РjРµС,PsСҫ РiРëР·РSP°СҫРµРµРSPSCП СҫР°СҫС,PsС,Рё
РiРµСҫРiРëРSPSPsРiРs РiРëРSPëРeРSPµРSPSCП Р°Р±Рs Р·Р°РiРsСҫС,СҫРµРµРSPSCП
РeР»С-РSC-СҫРSPs Р·РSP°СҫСҫ°РsС— РrРµРiСҫРµСҫСҫ-С— С,Р° РiРsСҫРiРë Р°РSPµРjС-С—. Рj
РrРsСҫР»С-РrРµРµРµРSPSC- РiР·СҫР»РёРё СҫСҫР°СҫС,Сҫ Р·Р°РiР°Р»Р»sРj 27840 РµС-РSPsРe,
СҫРeРёРj Р±СҫР»Рs РiРiРµСҫРµРµ РiСҫРёР·РSP°СҫРµРµРSPs РiРsСҫРjРsРSP°Р»СҫРSCҫ
С,РµСҫР°РiС-Сҫ РrР»Сҫ Р»С-РeСҫРiР°РSPSCП РµРSPRРsРjРµС,СҫС-РsР·Сҫ, С- Р·Р°
С—С...РSC-Рj СҫС,Р°РSPsРj СҫРiРsСҫС,РµСҫС-РiР°Р»Р»Рё РiСҫРsС,СҫРiРsРj РiРµСҫС-РsРrСҫ
РrРs 7 СҫРsРeС-Рi.

3023 РµС-РSPeР°Рj Р±СҫР»Рs РiСҫРё Р·РSP°СҫРµРµРµ РrС-С"РSPsРiРµСҫС, Сҫ
РrРsР·СҫРiР°РSPSC- 2 РjРi, 3371 РiР°Сҫ-С"РSC,СҫС- Р±СҫР»Рs РiСҫРё Р·РSP°СҫРµРµРµРµ
С-РSCёС- Р»С-РeР°СҫСҫСҫРeС- Р·Р°СҫРsР±Рё СҫС...РiР°Р»Р»sРµС- РrР»Сҫ
Р»С-РeСҫРiР°РSPSCП РµРSPRРsРjРµС,СҫС-РsР·Сҫ. Р—Р°РiР°Р»Р»sРµС
СҫРeРsСҫРёРiРsРiР°РSPµ СҫРiС-РiРiС-РrРSPsСҫРµРµРµРSPSCП СҫРёР·Р·РeРeС-Рi
РiРëРSPëРeРSPµРSPSCП РSPsРiРëС... РiРëРiР°РrРeС-Рi Р°РSPµРjС-С— Сҫ РiР°Сҫ-С"РSC,PsPe,
СҫРeС- РiСҫРё РµРµРjР°Р»Р» РrС-С"РSPsРiРµСҫС,, РiРsСҫС-РiРSCПSPs Р·
РiР°Сҫ-С"РSC,РeР°РjРё, СҫРeС- РiСҫРё РµРµРjР°Р»Р» Р»С-РSCёС- Р»С-РeР°СҫСҫСҫРeС-
Р·Р°СҫРsР±Рё СҫС...РiР°Р»Р»sРµС- РrР»Сҫ Р»С-РeСҫРiР°РSPSCП РµРSPRРsРjРµС,СҫС-РsР·Сҫ,
СҫС,Р°РSPsРiРëР»Рs 1,1 (Р"Р± 95%: 0,4-2,6). РёРeРsСҫРёРiРsРiР°РSPµ
СҫРiС-РiРiС-РrРSPsСҫРµРµРµРSPSCП СҫРёР·Р·РeРeС-Рi РiРëРSPëРeРSPµРSPSCП
РrРµРiСҫРµСҫС-С— Сҫ РiР°Сҫ-С"РSC,PsPe, СҫРeС- РiСҫРё РµРµРjР°Р»Р» Р»С-С"РSPsРiРµСҫС,,
РiРsСҫС-РiРSCПSPs Р· РiР°Сҫ-С"РSC,РeР°РjРё, СҫРeС- РiСҫРё РµРµРjР°Р»Р» Р»С-РSCёС-
Р»С-РeР°СҫСҫСҫРeС- Р·Р°СҫРsР±Рё СҫС...РiР°Р»Р»sРµС- РrР»Сҫ Р»С-РeСҫРiР°РSPSCП
РµРSPRРsРjРµС,СҫС-РsР·Сҫ, СҫС,Р°РSPsРiРëР»Рs 1,8 (Р"Р± 95 %: 0,3-9,4). РёРµ РjРsРµРµРSP°
РiРëРeР»»СҫСҫРё,Рё РSPµР·РSP°СҫРSPµ РiС-РrРiРëС°РµРµРSPSCП СҫРёР·Р·РeРeСҫ
РiРëРSPëРeРSPµРSPSCП РrРµРiСҫРµСҫС-С— Сҫ РiР°Сҫ-С"РSC,PsPe, СҫРeС-
РiСҫРё РµРµРjР°Р»Р» РiСҫ,Сҫ РrС-С"РSPsРiРµСҫС,, РiРsСҫС-РiРSCПSPs Р· РiР°Сҫ-С"РSC,РeР°РjРё,
СҫРeС- РiСҫРё РµРµРjР°Р»Р» РiСҫ,Сҫ С-РSCёС- Р»С-РeР°СҫСҫСҫРeС- Р·Р°СҫРsР±Рё
СҫС...РiР°Р»Р»sРµС- РrР»Сҫ Р»С-РeСҫРiР°РSPSCП РµРSPRРsРjРµС,СҫС-РsР·Сҫ.

Р»°СҫРjР°РeРsРeС-РSPµС,РёРeР°.

Р'СҫРjРsРeС,СҫРiРiР°РSPSCП

РµС-СҫР»Сҫ РiРµСҫРsСҫР»Р»СҫР»СҫРiРs РiСҫРё РµРµРµРµРjСҫ РrС-С"РSPsРiРµСҫС, СҫРiРëРrРeРs
С- РiРsРiРSC-СҫС,Сҫ РiСҫРjРsРeС,СҫС"С,СҫСҫСҫ. РҫР°РeСҫРёРjР°Р»Р»СҫР»РSP°
РeРsРSCҫРµРSPС,СҫР°Сҫ-Сҫ Сҫ РiРëСҫРsРiР°РSP°С,СҫС- РeСҫРiС- РrРsСҫСҫРiР°РSP°С,СҫСҫСҫ
РiСҫРё Р»Р»Р»Р»Р» РiРiРµСҫРµРµРµ РiС-СҫР»Сҫ РsРrРSPsСҫР»Р°Р·РsРiРs
РiРµСҫРsСҫР»Р» РiСҫРё РµРµРµРµРjСҫ С- СҫС,Р°РSPsРiРëС,Сҫ 47 РSPi/РjР». Р'С-РsРrРsСҫС,
СҫРiРiРSC-СҫС,Сҫ СҫС,Р°РSPsРiРëС,Сҫ РiСҫРё Р»Р»Р»Р»Р» Р»Р»РSPs 91 %.
Р»°СҫРjР°РeРsРeС-РSPµС,РёРeР° РrС-С"РSPsРiРµСҫС,Сҫ Р·Р°Р»Р»Р»Р»Р»Р»Сҫ,Сҫ РiС-Рr РrРsР·Рё
Рi РrС-Р°РiР°РSPSC- РrРsР· 1-8 РjРi.

P PsP·PiPsPrC-P»

P"С-С" PSPsPiPμCfC, P·PIBf™ CIP·CfC"С,СHСfCfC P·C- CfPëCfPSPiP°С,PePsPiPëPj P°P»СHfP±CfPjC-PSPsPj C,P° PSPμ P·PIBf™ CIP·CfC"С,СHСfCfC C-P· PiP»PsP±CfP»C-PSPsPj, C%Ps P·PIBf™ CIP·CfC" CfC,P°С,PμPIC- CfC,PμCfPсC—PrPë (P"Р—PŸPŸ), P°P±Ps C-P· PiP»PsP±CfP»C-PSPsPj, C%Ps P·PIBf™ CIP·CfC" PePsCfC,PëPePsC—PrPë (P"Р—Pљ). 10 % PIC-Pr P·P°PiP°P»СHfPSPсC— PePsPSC†PμPSC,CfP°C†C-C— PrC-C" PSPsPiPμCfC,Cf Cf CfPëCfPSPiP°С,C†C- PeCfPсPIC- P·PSP°С...PsPrCfC,СHСfCfC Cf PiPëPiP»CfPrC- PIC-P»СHfPSPsPiPs CfC,PμCfPсC—PrCf, P° 90 % - PSPμCfPiPμC†PëC,,C-СfPSPs P·PIBf™ CIP·P°PSC- P· P°P»СHfP±CfPjC-PSPsPj. PhC†PμPiPëPrPSPëP№ PsP±Bf™ C" Pj CfPсP·PiPsPrC-P»Cf (Vq/F) PrC-C" PSPsPiPμCfC,Cf CfC,P°PSPsPiPëC,СH 40 P».

PfPμC,P°P±PsP»C-P·Pj

P"С-С" PSPsPiPμCfC, PiPsPiPSC-CfC,Сf PjPμC,P°P±PsP»C-P·CfC"С,СHСfCfC PIC-PrPsPjPëPjPë CëP»CfC...P°PjPë PjPμC,P°P±PsP»C-P·PjCf CfC,PμCfPсC—PrC-PI, P· CfC,PIPsCfPμPSPSCfPj PiPμCfPμPiP°P¶PSPs PμPSPrPsPeCfPëPSPsP»PsPiC-C†PSPs PSPμP°PeC,PëPiPSPëC... PjPμC,P°P±PsP»C-C,C-PI. Pk° PiC-PrCfC,P°PIC- PrPsCfP»C-PrP¶PμPSCH in vitro C,P° in vivo CYP3A4 вf" PiPsP»PsPiPSPëP№ C,,PμCfPjPμPSC,, P·P°P»CfC†PμPSPëP№ Cf PjPμC,P°P±PsP»C-P·Pj PrC-C" PSPsPiPμCfC,Cf. PjC- PjPμC,P°P±PsP»C-C,Pë PrCfP¶Pμ CëPiPëPrPePs PiPëPiPsPrCfC,СHСfCfC P· PiP»P°P·PjPë PeCfPсPIC- Cf C,P°PePëP№ CfPiPsCfC-P±, C%Ps PrPsPjC-PSCfCfC†PsCf C,,CfP°PeC†C-C"Сf Cf PiP»P°P·PjC- PeCfPсPIC- C" PrC-C" PSPsPiPμCfC, Cf PSPμP·PjC-PSPμPSPsPjCf PiPëPiP»CfPrC-.

PëPiPëPrPeC-CfC,СH PeP»C-CfPμPSCfCf (Cl/F) P·C- CfPëCfPSPiP°С,PePë PeCfPсPIC- CfC,P°PSPsPiPëC,СH 64 PjP»/C...PI.

P'PëPiPμPrPμPSPSCfC

P C-PIPμPSCH PrC-C" PSPsPiPμCfC,Cf PI CfPëCfPSPiP°С,C†C- PeCfPсPIC- P·PSPëP¶CfC"С,СHСfCfC PrPiPsC,,P°P·PSPs. PљC-PSC†PμPiP° C,,P°P·P° PiPëPiPμPrPμPSPSCfC C...P°CfP°PeC,PμCfPëP·CfC"С,СHСfCfC PiPμCfC-PsPrPsPj PSP°PiC-PIPiPëPiPμPrPμPSPSCfC, C%Ps CfC,P°PSPsPiPëC,СH PiCfPëP±P»PëP·PSPs 9-10 PiPsPrPëPS. P"С-С" PSPsPiPμCfC, PiPëPiPsPrPëC,СHСfCfC Cf C,,PsCfPjC- PjPμC,P°P±PsP»C-C,C-PI C-P· CfPμC†PμCf C,P° PeP°P»PsPj Cf CfPiC-PIPIC-PrPSPsCëPμPSPSC- PiCfPëP±P»PëP·PSPs 3:1 PiC-CfP»Cf PiPμCfPсCfP°P»СHfPSPsPiPs PiCfPëP№PsPjCf PI PrPsP·C- 0,1 PjPi/PePi. PμPμCfC-PsPr PSP°PiC-PIPiPëPiPμPrPμPSPSCfC PjPμC,P°P±PsP»C-C,C-PI P· CfPμC†PμCf CfC,P°PSPsPiPëC,СH PiCfPëP±P»PëP·PSPs 14 PiPsPrPëPS.

PμC-CfP»Cf PiPμCfPсCfP°P»СHfPSPsPiPs PiCfPëP№PsPjCf 86 % PiPiPμPrPμPSPсC— PrPsP·Pë PiPëPiPsPrPëC,СHСfCfC P· PsCfPiP°PSC-P·PjCf Cf PjPμP¶P°С... 6 PrPSC-PI, P±C-P»СHСëP° C†P°CfC,PëPSP° C†C-C"С— PeC-P»СHfPePsCfC,C- PiPëPiPsPrPëC,СHСfCfC Cf PiPμCfCëC- 24 PiPsPrPëPSPë, PiPsP»PsPiPSPëPj C†PëPSPsPj C-P· CfPμC†PμCf.

PŸC,P°PS CfC-PIPSPsPiPë

PαP°CfPjP°PePsPeC-PSPμC,PëPeP° PrC-C" PSPsPiPμCfC,Cf PSPμ P·P°P»PμP¶PëC,СH PIC-Pr CfC-PIPSCfC P"Р—PŸPŸ. PμCfPë C%PsPrPμPSPSPsPjCf PiCfPëP№PsPjC- PePsPSC†PμPSC,CfP°C†C-Cf CfPμC†PμPiPëPSPë Cf CfPëCfPSPiP°С,C†C- PeCfPсPIC- P·CfPсCfC,P°С" PiCfPëP±P»PëP·PSPs PI 1,24 CfP°P·P°, PrPsCfCfPiP°CfC†Pë CfC-PIPSPsPiP°P¶PSPsPiPs CfC,P°PSC† C†PμCfPμP· 4 PrPSC- P·P°CfC,PsCfCfPiP°PSPSCfC. PαP°CfPjP°PePsPeC-PSPμC,PëPeP° PrC-C" PSPsPiPμCfC,Cf PiC-CfP»Cf PiPsPIC,PsCfPSPsPiPs

P·P°CÍC,PsCÍCfPIP°PSPSCЦ PrC-C"PSPsPiPµCÍC,Cr, C,P°P±P»PµC,PsPe 2 PjPi, PjPsP¶Pµ
P±CfC,Pë PíPµCЦPµPrP±P°C±PµPSP° PSP° PíC-PrCÍC,P°PIC- PrP°PSPëC... C%PsPrPs
C,,P°CЦPjP°PePsPeC-PSPµC,PëPePë PsPrPSC-C"C— PrPsP·Pë.

PαP°CЦPjP°PePsPeC-PSPµC,PëPeP° PI PsCÍCfPsP±P»PëPIPëC... PíCЦCfPíP°C... PíP°C†C-C"PSC,C-PI

PJ PíP°C†C-C"PSC,C-PI C-P· PíPsCЦCfCεPµPSPSCЦPjPë C,,CfPSPeC†C-C— PSPëCЦPsPe
C,,P°CЦPjP°PePsPeC-PSPµC,PëPeCf PíCЦPµPíP°CЦP°C,Cf CP°PIC-CÍ, C,P°P±P»PµC,PsPe 2 PjPi,
PSPµ PIPëPIC±P°P»Pë.

PJ PíP°C†C-C"PSC,C-PI C-P· PíPsCЦCfCεPµPSPSCЦPjPë C,,CfPSPeC†C-C— PíPµC±C-PSPePë
C,,P°CЦPjP°PePsPeC-PSPµC,PëPeCf PíCЦPµPíP°CЦP°C,Cf PŸP°PIC-CÍ, C,P°P±P»PµC,PsPe 2 PjPi,
PSPµ PIPëPIC±P°P»Pë.

РљР»С-РSC-С±РSC- С...Р°СЦР°РeС,РµСЦРëСÍС,РëРeРë.

РµРsРeР°Р·Р°РSPSCЦ. P>C-РeCfPIP°PSPSCЦ PµPSPPrPsPjPµC,ЦЦC-РsP·Cf.

РµСЦРsС,РëPíРsРeР°Р·Р°РSPSCЦ. PµCЦPµPíP°CЦP°C, PŸP°PIC-CÍ PSPµ CÍP»C-Pr
P·P°CÍC,PsCÍCfPICfPIP°C,Pë Cr CЦP°P·C- PSP°CЦPIPSPsCÍC,C- P±CfPrCЦ-CЦPеPsPiPs C-P·
PSPëP¶C±PµP·P°P·PSP°C±PµPSPëC... CÍC,P°PSC-PI P°P±Ps P·P°C...PIPsCЦCЦPIP°PSCЦ. PíCЦ
C-PSC,,PsCЦPjP°C†C-CЦ C±P°CÍC,PePsPIPs PsC,CЦPëPjP°PSP° PSP° PíC-PrCÍC,P°PIC-
P·P°CÍC,PsCÍCfPIP°PSPSCЦ C-PSCεPëC... PíCЦPµPíP°CЦP°C,C-PI, C%Ps PjC-CÍC,CЦC,ЦЦ
C,C-P»CЦPëPë PíCЦPsPiPµCÍC,PsPiPµPS. PíPëC%Ps P±CfPrCЦ-CЦPëPëPñ C-P· C†PëC...
CÍC,P°PSC-PI P°P±Ps P·P°C...PIPsCЦCЦPIP°PSCЦ PIPëPSPëPëP°C" PIPíPµCЦCεPµ PíC-Pr
C±P°CÍ P·P°CÍC,PsCÍCfPIP°PSPSCЦ PíCЦPµPíP°CЦP°C,Cf PŸP°PIC-CÍ, PíCЦPëPñPsPj
PíCЦPµPíP°CЦP°C,Cf CÍP»C-Pr PSPµPíP°PñPSPs PíCЦPëPíPëPSPëC,Pë:

- PIPµPSPsP·PSP° C,CЦPsPjP±PsPµPjP±PsP»C-CЦ PI P°PeC,PëPIPSC-Pñ C,,PsCЦPjC-;

- P°CЦC,РµCЦC-P°P»CЦPSC- P°P±Ps PeP°CЦPrC-РsPIP°CÍPëCfP»CЦCЦPSC-
P·P°C...PIPsCЦCЦPIP°PSPSCЦ PSPëPSC- P°P±Ps PI P°PSP°PjPSPµP·C- (PSP°PíCЦPëPëP»P°Pr
C-PSC,,P°CЦPeC, PjC-РsPeP°CЦPrP°, C†PµCЦPµP±CЦPsPIP°CÍPëCfP»CЦCЦPSP° PíPsPrC-CЦ,
C-CεPµPjC-C±PSP° C...PIPsCЦPsP±P° CÍPµCЦC†CЦ);

- C†CfPeCЦPsPIPëPñ PrC-P°P±PµC, P· CfCЦP°P¶PµPSPSCЦPj CÍCfPrPëPS;

- C,CЦP¶PeC- P·P°C...PIPsCЦCЦPIP°PSPSCЦ PíPµC±C-PSPePë PSPëPSC- P°P±Ps C—C...
PSP°CЦPIPS-СÍC,ЦЦ PI P°PSP°PjPSPµP·C-, PíPsPePë PíPsPeP°P·PSPëPëPë C,,CfPSPeC†C-C—
PíPµC±C-PSPePë PSPµ PíPsPIPµCЦPSCfC,ЦЦCÍCЦ PrPs PSPsCЦPjPë;

- PíCfC...P»PëPSPë PíPµC±C-PSPePë PSPëPSC- P°P±Ps PI P°PSP°PjPSPµP·C-
(PrPsP±CЦPsCЦPëC-CÍPSC- P°P±Ps P·P»PsCЦPëC-CÍPSC-);

- PIC-PrPsPjC- P°P±Ps PíC-PrPsP·CЦCЦPIP°PSC- P·P»PsCЦPëC-CÍPSC- PíCfC...P»PëPSPë,
P·P°P»PµP¶PSC- PIC-Pr CÍC,P°C,РµPIPëC... PíPsCЦPjPsPSC-PI;

- PIP°PíC-PSP°P»CЦPSP° PeCЦPsPIPsC,РµC±P° PSPµP·BЦ™ CЦCÍCfPsPIP°PSPsC—
PµC,C-РsP»PsPíC-C—;

- PíC-PrPIPëC%PµPSP° C±CfC,P»PëPIC-CÍC,ЦЦ PrPs PrC-CЦC±PsC— CЦPµC±PsPIPëPSPë

P°P±Ps PrPs P±CfPrCH-CIIPePsC— P· PrPsPiPsPjC-P¶PSPëC... C¶PµC±PsPIPëPS
PiC¶PµPiP°C¶P°C,Cr (PrPëPI. C¶PsP·PrC-P» B«PŸPeP»P°PrB»).

**P°P°C°PjPsPrC-CI P· C-PSCëPëPjPë P»C-PeP°C¶CfCHPePëPjPë P·P°CfPsP±P°PjPë C,P°
C-PSCëC- PIPëPrPë PIP·P°C°PjPsPrC-PNë.**

PµC¶PëPjC-C,PeP°: PrP»CI PIPëCIPIP»PµPSPSC¶ PjPsP¶P»PëPIPëC... PIP·P°C°PjPsPrC-PNë
CfP»C-Pr PsP·PSP°PNëPsPjPëC,PëCfC¶ P· C-PSCfC,C¶CfPeC†C-CIIPjPë PrP»CI
PjPµPrPëC±PSPsPiPs P·P°CfC,PsCfCfPIP°PSPSC¶ P»C-PeP°C¶CfCHPePëC... P·P°CfPsP±C-PI,
C%Ps P·P°CfC,PsCfPsPICfCHC,CHCfC¶ CfCfPiCfC,PSCHPs.

P°PiP»PëPI C-PSCëPëC... PiC¶PµPiP°C¶P°C,C-PI PSP° PŸP°PIC-Cf

PµC¶PsPiPµCfC,PsPiPµPSPë, PIPeP»CHC±P°CHC±Pë PrC-C°PSPsPiPµCfC,,
PjPµC,P°P±PsP»C-P·CfCHC,CHCfC¶ PiPsP»PsPIPSPëPj C±PëPSPsPj CfPëCfC,PµPjPsC¶
C†PëC,PsC...C¶PsPjCr P 450 3P¶4 (CYP3A4), C%Ps C¶PsP·C,P°CëPsPIP°PSP° Cr
CfP»PëP·PsPIC-PNë PsP±PsP»PsPSC†C- PePëCëPµC±PSPëPeCf C,P° PI PiPµC±C-PSC†C-. PŸPsPjCr
C-PSPrCfPeC,PsC¶Pë P°P±Ps C-PSPiC-P±C-C,PsC¶Pë CYP3A4 PjPsP¶CfC,CH PIPiP»PëPIP°C,Pë
PSP° PjPµC,P°P±PsP»C-P·Pj PiC¶PsPiPµCfC,PsPiPµPSCf.

P—P±C-P»CHCëPµPSPSC¶ PeP»C-C¶PµPSCfCf CfC,P°C,PµPIPëC... PiPsC¶PjPsPSC-PI
C±PµC¶PµP· C-PSPrCfPeC†C-CH C,,PµC¶PjPµPSC,C-PI PjPsP¶Pµ P·PjPµPSCëPëC,Pë
C,PµC¶P°PiPµPIC,PëC±PSPëPNë PµC,,PµPeC, PiC¶PµPiP°C¶P°C,Cr PŸP°PIC-Cf C-
PiC¶PëP·PIPµCfC,Pë PrPs PSPµP±P°P¶P°PSPëC... PµC,,PµPeC,C-PI, PSP°PiC¶PëPeP»P°Pr PrPs
P·PjC-PS C...P°C¶P°PeC,PµC¶Cf PjPµPSCfC,C¶CfP°P»CHPSPsC— PeC¶PsPIPsC,PµC±C-.

P—PjPµPSCëPµPSPSC¶ PeP»C-C¶PµPSCfCf CfC,P°C,PµPIPëC... PiPsC¶PjPsPSC-PI C±PµC¶PµP·
PiC¶PëPiPSC-C±PµPSPSC¶ C,,PµC¶PjPµPSC,Cr PjPsP¶Pµ P·P±C-P»CHCëPëC,Pë PIPiP»PëPI
PrC-C°PSPsPiPµCfC,Cr C- PiC¶PëP·PIPµCfC,Pë PrPs C¶PsP·PIPëC,PeCf PiPsP±C-C±PSPëC...
C¶PµP°PeC†C-PNë.

P PµC±PsPIPëPSPë, C%Ps PiC-PrPIPëC%CrCHC,CH PeP»C-C¶PµPSCf CfC,P°C,PµPIPëC...
PiPsC¶PjPsPSC-PI (P·PSPëP¶PµPSPSC¶ PµC,,PµPeC,PëPIPSPsCfC,C- CëP»C¶C...PsPj
C-PSPrCfPeCfPIP°PSPSC¶ C,,PµC¶PjPµPSC,C-PI), PSP°PiC¶PëPeP»P°Pr: C,,PµPSC-C,PsC—PS,
P±P°C¶P±C-C,CfC¶P°C,Pë, PiC¶PëPjC-PrPsPS, PeP°C¶P±P°PjP°P·PµPiC-PS,
C¶PëC,,P°PjPiC-C†PëPS, P° C,P°PePsP¶, PjPsP¶P»PëPIPs, PsPeCfPeP°C¶P±P°P·PµPiC-PS,
C,PsPiC-C¶P°PjP°C,, C,,PµP»CHP±P°PjP°C,, PiC¶PëP·PµPsC,,CfP»CHPIC-PS C,P° P·P°CfPsP±Pë,
C%Ps PjC-CfC,C¶C,CH P·PIC-C¶PsP±C-PNë (*Hypericum perforatum*).

P†PSPrCfPeC†C-C¶ C,,PµC¶PjPµPSC,C-PI PjPsP¶Pµ CfPiPsCfC,PµC¶C-PiP°C,PëCfC¶ PIP¶Pµ
PiC-CfP»C¶ PrPµPeC-P»CHPePsC... PrPSC-PI C,PµC¶P°PiC-C—. P¶P°PeCfPëPjP°P»CHPSP°
C-PSPrCfPeC†C-C¶ C,,PµC¶PjPµPSC,C-PI P·P°PiP°P»PsPj PIPëCIPIP»C¶C°C,CHCfC¶
C±PµC¶PµP· PrPµPeC-P»CHPeP° C,PëP¶PSC-PI. P†PSPrCfPeC†C-C¶ C,,PµC¶PjPµPSC,C-PI
PjPsP¶Pµ C,C¶PëPIP°C,Pë PrPs 4 C,PëP¶PSC-PI PiC-CfP»C¶ PiC¶PëPiPëPSPµPSPSC¶
C,PµC¶P°PiC-C—.

P°PiP»PëPI C-PSPrCfPeC,PsC¶P° CYP 3P¶4 C¶PëC,,P°PjPiC-C†PëPSCf
PrPsCfP»C-PrP¶CfPIP°PICfC¶ Cr P·PrPsC¶PsPIPëC... P¶C-PSPsPe Cf
PiPsCfC,PeP»C-PjP°PeC,PµC¶PëC±PSPsPjCr PiPµC¶C-PsPrC-. P¶PSPsC±P°CfPSPµ
P·P°CfC,PsCfCfPIP°PSPSC¶ C¶PëC,,P°PjPiC-C†PëPSCf P· C,P°P±P»PµC,PsPIP°PSPsC¶

C,,PsCḥPjPsCḥ PμCÍC,CḥP°PrC-PsP»CÍ PIP°P»PμCḥP°C,CÍ/PrC-C"PSPsPiPμCÍC,CÍ
PíCḥPëP·PIPμP»Ps PrPs P·PSP°C‡PSPsPiPs P·PSPëP¶PμPSPSCÍ CḥC-PIPSPsPIP°P¶PSPsC—
PePsPSC‡PμPSC,CḥP°C‡C-C— C,P° CÍPëCÍC,PμPjPSPsPiPs PIPiP»PëPICÍ PrC-C"PSPsPiPμCÍC,CÍ
C,P° PμCÍC,CḥP°PrC-PsP»CÍ. PŸPëCÍC,PμPjPSPëPNë PIPiP»PëPI PrC-C"PSPsPiPμCÍC,CÍ C,P°
PμCÍC,CḥP°PrC-PsP»CÍ CÍ CḥC-PIPSPsPIP°P¶PSPsPjCÍ CÍC,P°PSC-, PIPëPjC-CḥCÍPSPëPNë P·P°
AUC (0 бҕ" 24 PiPsPrPëPSPë), P·PjPμPSCëPëPICÍCÍ PSP° 83 % C,P° 44 % PIC-PrPiPsPIC-PrPSPs.

P PμC‡PsPIPëPSPë P· CḥC-P·PSPëPj PIPiP»PëPIPsPj PSP° PeP»C-CḥPμPSCÍ CÍC,P°C,PμPIPëC...
PiPsCḥPjPsPSC-PI.

PḥPrPSPsC‡P°CÍPSPμ P·P°CÍC,PsCÍCÍPIP°PSPSCÍ P·C- CÍC,P°C,PμPIPëPjPë
PiPsCḥPjPsPSP°PjPë PIPμP»PëPePsC— PeC-P»CḥPePsCÍC,C- PePsPjP±C-PSP°C‡C-PNë
C-PSPiC-P±C-C,PsCḥC-PI P'P‡P>-PíCḥPsC,PμP°P·Pë C,P°
PSPμPSCÍPeP»PμPsP·PëPrPSPëC... C-PSPiC-P±C-C,PsCḥC-PI P·PIPsCḥPsC,PSPsC—
C,CḥP°PSCÍPeCḥPëPíC,P°P·Pë, CÍ PiPsC"PrPSP°PSPSC- P· PePsPjP±C-PSP°C‡C-CÍPjPë
C-PSPiC-P±C-C,PsCḥC-PI PIC-CḥCÍCÍCÍ PiPμPiP°C,PëC,CÍ PŸ, PjPsP¶Pμ
P·P±C-P»CḥCëPëC,Pë P°P±Ps P·PjPμPSCëPëC,Pë CḥC-PIPμPSCḥ
PíCḥPsPiPμCÍC,PëPSCÍ PI PiP»P°P·PjC- PeCḥPsPIC-. PŸCÍPeCÍPiPSPëPNë PIPiP»PëPI
C‡PëC... P·PjC-PS PjPsP¶Pμ P±CÍC,Pë PeP»C-PSC-C‡PSPs P·PSP°C‡CÍC°PëPj CÍ
PrPμCÍPePëC... PIPëPiP°PrPeP°C....

P PμC‡PsPIPëPSPë, C°Ps P·PSPëP¶CÍCḥC,Cḥ PeP»C-CḥPμPSCÍ CÍC,P°C,PμPIPëC...
PiPsCḥPjPsPSC-PI (C-PSPiC-P±C-C,PsCḥPë C,,PμCḥPjPμPSC,C-PI).

P" C-C"PSPsPiPμCÍC, C" CÍCÍP±CÍC,CḥP°C,PsPj C‡PëC,PsC...CḥPsPjCÍ P450 (CYP) 3A4.

PḥP»C-PSC-C‡PSP° P·PSP°C‡CÍC°C-CÍC,Cḥ PiPsC,PμPSC‡C-PNëPSPëC... PIP·P°C" PjPsPrC-PNë
P· C-PSPiC-P±C-C,PsCḥP°PjPë C,,PμCḥPjPμPSC,C-PI P·P°P»PëCëP°C"C,CḥCÍCÍ
PSPμPIC-PrPsPjPsCḥ.

PḥPrPSPsC‡P°CÍPSPμ P·P°CÍC,PsCÍCÍPIP°PSPSCÍ CÍPëP»CḥPSPëC...
C-PSPiC-P±C-C,PsCḥC-PI CYP3A4 PjPsP¶Pμ P·P±C-P»CḥCëCÍPIP°C,Pë PiP»P°P·PjPsPIC-
PePsPSC‡PμPSC,CḥP°C‡C-C— PrC-C"PSPsPiPμCÍC,CÍ.

PḥPrPSPsC‡P°CÍPSPμ P·P°CÍC,PsCÍCÍPIP°PSPSCÍ C-P· CÍPëP»CḥPSPëPj
C-PSPiC-P±C-C,PsCḥPsPj C,,PμCḥPjPμPSC,CÍ CYP3A4 PePμC,PsPePsPSP°P·PsP»PsPj
PíCḥPëP·PIPsPrPëP»Ps PrPs PíC-PrPIPëC°PμPSPSCÍ CÍ 2,9 CḥP°P·P° AUC (0 бҕ" 24
PiPsPrPëPSPë) PrC-C"PSPsPiPμCÍC,CÍ PI CḥC-PIPSPsPIP°P¶PSPsPjCÍ CÍC,P°PSC-.
PḥPrPSPsC‡P°CÍPSPμ P·P°CÍC,PsCÍCÍPIP°PSPSCÍ P· PiPsPjC-CḥPSPëPj
C-PSPiC-P±C-C,PsCḥPsPj PμCḥPëC,CḥPsPjC-C‡PëPSPsPj PíCḥPëP·PIPsPrPëP»Ps PrPs
PíC-PrPIPëC°PμPSPSCÍ CÍ 1,6 CḥP°P·P° AUC (0 бҕ" 24 PiPsPrPëPSPë) PrC-C"PSPsPiPμCÍC,CÍ
CÍ CḥC-PIPSPsPIP°P¶PSPsPjCÍ CÍC,P°PSC-.

P·PiP»PëPI PíCḥPμPiP°CḥP°C,CÍ PŸP°PIC-CÍ PSP° C-PSCëC- P»C-PeP°CḥCÍCḥPeC-
P·P°CÍPsP±Pë

P—P° CḥPμP·CÍP»CḥC,P°C,P°PjPë PrPsCÍP»C-PrP¶PμPSCḥ C-PSPiC-P±CÍPIP°PSPSCÍ *in vitro*,
PeP»C-PSC-C‡PSPs P·PSP°C‡CÍC°P° PIP·P°C" PjPsPrC-CÍ PrC-C"PSPsPiPμCÍC,CÍ C-P·
C-PSCëPëPjPë PíCḥPμPiP°CḥP°C,P°PjPë, PjPμC,P°P±PsP»C-P·Pj CÍPePëC...
PsPiPsCÍPμCḥPμPrPePsPICÍC"C,CḥCÍCÍ C,,PμCḥPjPμPSC,P°PjPë C‡PëC,PsC...CḥPsPjCÍ P450,
C" PjP°P»PsPNëPjPsPIC-CḥPSPsCḥ.

P·P·P·C”PjPsPrC-CI P· C...P°CḡC±PsPIPëPjPë PiCḡPsPrCfPeC,P°PjPë

P·P¶PëPIP°PSPSCI C—P¶C- P· PIPëCfPsPePëPj PIPjC-CfC,PsPj P¶PëCḡC-PI PSPµ
PIPiP»PëPIP°P»Ps PSP° P±C-PsPrPsCfC,CfPiPSC-CfC,Ch PiCḡPµPiP°CḡP°C,Cf PŸP°PIC-Cf.

P»P°P±PsCḡP°C,PsCḡPSC- C,PµCfC,Pë

PµCḡPëPNëPsPj PiCḡPsPiPµCfC,PsPiPµPSC-PI PjPsP¶Pµ PIPiP»PëPSCfC,Pë PSP°
CḡPµP·CfP»ChC,P°C,Pë PrPµCfPePëC... P»P°P±PsCḡP°C,PsCḡPSPëC... P°PSP°P»C-P·C-PI,
P·PsPeCḡPµPjP° PSP° P±C-PsC...C-PjC-C±PSC- PiP°CḡP°PjPµC,CḡPë PiPµC±C-PSPëPë,
C%oPëC,PsPIPëPrPSPsC— P·P°P»PsP·Pë, C,,CfPSPëCfC-C— PSPëCḡPsPe C,P°
PSP°PrPSPëCḡPePsPIPëC... P·P°P»PsP·, CḡC-PIPSC- P±C-P»PeC-PI (PSPsCfC-C-PI) Cf
PiP»P°P·PjC- PeCḡPsPIC- (PSP°PiCḡPëPeP»P°Pr, P“P—Pḡ C,P° C,,CḡP°PeCfC-C—
P»C-PiC-PrC-PI/P»C-PiPsPiCḡPsC,PµC—PrC-PI), PiP°CḡP°PjPµC,CḡPë PjPµC,P°P±PsP»C-P·PjCf
PICfPiP»PµPIPPrC-PI C,P° PiPsPeP°P·PSPëPePë PePsP°PiCfP»CfCfC-C— PNë
C,,C-P±CḡPëPSPsP»C-P·Cf. P—PjC-PSPë P·P°P·PIPëC±P°PNë P·P°P»PëCεP°CḡC,ChCfCfCf Cf
PjPµP¶P°C... P»P°P±PsCḡP°C,PsCḡPSPsC— PSPsCḡPjPë.

PḡCfPsP±P»PëPIP°CfC,C- P·P°CfC,PsCfC±PIP°PSPSCI.

P—P°CfC,PµCḡPµP¶PµPSPSCI.

PḡCfPeC-P»ChPePë CP°PIC-Cf - PiCḡPµPiP°CḡP°C,, C%oPs PjC-CfC,PëC,Ch C,C-P»ChPePë
PiCḡPsPiPµCfC,PsPiPµPS, PIPiP°P¶P°C”C,ChCfCfCf, C%oPs PsCfPsP±P»PëPIC-
P·P°CfC,PµCḡPµP¶PµPSPSCI C,P° P·P°C...PsPrPë P±PµP·PiPµPePë C%oPsPrPs
P·P°CfC,PsCfCfPIP°PSPSCI PiCḡPµPiP°CḡP°C,C-PI, C%oPs PjC-CfC,CfC,Ch C,C-P»ChPePë
PiCḡPsPiPµCfC,PsPiPµPS, C,P°PePsP¶ CfC,PsCfCfCḡC,ChCfCfCf PiCḡPµPiP°CḡP°C,Cf
CP°PIC-Cf, C...PsC±P° PSPµ PICfC- P·P°CfC,PµCḡPµP¶PµPSPSCI C,P° P·P°PiPsP±C-P¶PSC-
P·P°C...PsPrPë T’CḡCfPSC,CfCḡC,ChCfCfCf PSP° PIC-PrPiPsPIC-PrPSPëC...
CḡPµP·CfP»ChC,P°C,P°C... PeP»C-PSC-C±PSPëC... PrPsCfP»C-PrP¶PµPSCḡ C,P°P±P»PµC,PsPe,
CfPeC- PjC-CfC,CfC,Ch 2 PjPi PrC-C”PSPsPiPµCfC,Cf.

PiPeC%oPs P±CfPrCh-CfPePëPNë C-P· P·P°P·PSP°C±PµPSPëC... PSPëP¶C±Pµ
CfC,P°PSC-PI/C,,P°PeC,PsCḡC-PI CḡPëP·PëPeCf, PiCḡPëCfCfC,PSC- P°P±Ps
PiPsPiC-CḡCεCfCḡC,ChCfCfCf, PI C-PSPPrPëPIC-PrCfP°P»ChPSPsPjCf PiPsCḡCfPrPeCf PjP°C”
P±CfC,Pë PiCḡPsPIPµPrPµPSPëPNë P°PSP°P»C-P· CfPiC-PIPIC-PrPSPsCεPµPSPSCI
CḡPëP·PëPe/PePsCḡPëCfC,Ch PiPµCḡPµPr PiPsC±P°C,PePsPj P°P±Ps
PiCḡPsPrPsPIP¶PµPSPSCI Pj P·P°CfC,PsCfCfPIP°PSPSCI PiCḡPµPiP°CḡP°C,Cf PŸP°PIC-Cf.

PŸCfP¶PeC- PjP°C,PePsPIC- PeCḡPsPIP°C,PµC±C-

PḡP°C,PePsPIP° PeCḡPsPIP°C,PµC±P°, PSP°PiCḡPëPeP»P°Pr, Cf P¶C-PSPsPe P·
P°PrPµPSPsPjC-PsP·PsPj PjP°C,PePë P°P±Ps P»PµPNëPsPjC-PsPjPsCḡ PjP°C,PePë PjPsP¶Pµ
P·P±C-P»ChCεCfPIP°C,PëCfCfCf PiCḡPë P·P°CfC,PsCfCfPIP°PSPSC- PiCḡPµPiP°CḡP°C,Cf
CP°PIC-Cf. PiPeC%oPs PeCḡPsPIP°C,PµC±P° PIPëCḡP°P¶PµPSP° C- PSPµ
PiCḡPëPiPëPSCfC”C,ChCfCfCf PiCḡPsC,CfPiPsPj C,CḡPëPIP°P»PsPiPs C±P°CfCf, PIPsPSP°
PjPsP¶Pµ PiCḡPëP·PIPµCfC,Pë PrPs P°PSPµPjC-C— (Cf PrPµCfPePëC... PIPëPiP°PrPeP°C...
C,CfP¶PePsC—). Pj C,P°PePsPjCf CḡP°P·C- PiPsC,CḡC-P±PSPs CḡPsP·PiP»CfPSCfC,Pë
PiPëC,P°PSPSCI PiCḡPs PiCḡPëPiPëPSPµPSPSCI PiCḡPëPNëPsPjCf PiCḡPµPiP°CḡP°C,Cf.

P—PjC-PSP° C...P°CḡP°PeC,PµCḡCf PeCḡPsPIP°C,PµC±C-

P>C-PeCfPIP°PSPSCЦ PrC-C"PSPPiPμCfC,PsPj, C,P°P±P»PμC,PeP°PjPë PiPs 2 PjPi, PIPiP»PëPIP°C" PSP° C...P°CfP°PeC,PμCf PjPμPSCfC,CfCfP°P»CHPSPsC— PeCfPsPIPsC,PμC±C- Cr P±C-P»CHC€PScfC,C- P¶C-PSPsPe (PrPëPI. CfPSP·PrC-P) B«PμPsP±C-C±PSC- CfPμP°PeC†C-C-B»).

PiPëCfPeCfP»CЦC,PsCfPSC- PiPsCfCfC€PμPSPSCЦ

PkP° PiC-PrCfC,P°PIC- CfPμP·CfP»CHC,P°C,C-PI PμPiC-PrPμPjC-PsP»PsPiC-C±PSPëC... PrPsCfP»C-PrP¶PμPSCH PIPëCЦPIP»PμPSPs PSPμPIPμP»PëPeCf PeC-P»CHPeC-CfC,CH PrP°PSPëC... C%oPsPrPs C-CfPSCfPIP°PSPSCЦ P·PIBf™ CЦP·PeCf PjC-P¶ P·P°CfC,PsCfCfPIP°PSPSCЦPj PiCfPμPiP°CfP°C,C-PI, C%oPs PjC-CfC,CЦC,CH C,C-P»CHPePë PiCfPSPiPμCfC,PsPiPμPS, C- PiC-PrPIPëC%oPμPSPSCЦPj CfPëP·PëPeCf CfPSP·PIPëC,PeCf C-PSC,,P°CfPeC,Cf PjC-PsPeP°CfPrP° P°P±Ps C†PμCfPμP±CfP°P»CHPSPsC— C,CfPSPjP±PsPμPjP±PsP»C-C—. P PëP·PëPe PeP°CfPrC-PsPIP°CfPeCfP»CЦCfPSPëC... C- C†PμCfPμP±CfP°P»CHPSPëC... CЦPIPëC%o C€PIPëPrC€Pμ PiPsPIBf™ CЦP·P°PSPëPNë P· PIC-PePsPj, P°CfC,PμCfC-P°P»CHPSPsCf PiC-PiPμCfC,PμPSP·C-C"CF C- PiP°P»C-PSPSCЦPj. Pj P¶C-PSPsPe P· PiC-PiPμCfC,PμPSP·C-C"CF CfPëP·PëPe CfPSP·PIPëC,PeCf C-PSCfCfP»CHC,Cf PjPsP¶Pμ PrPμC%oPs P·P±C-P»CHC€CfPIP°C,PëCfCЦ PiCfPë P·P°CfC,PsCfCfPIP°PSPSC- PiCfPμPiP°CfP°C,C-PI, C%oPs PjC-CfC,CЦC,CH C,C-P»CHPePë PiCfPSPiPμCfC,PsPiPμPS.

P" PμCЦPeC- PrPsCfP»C-PrP¶PμPSPSCЦ CfPIC-PrC†P°C,CH PiCfPs C-CfPSCfPIP°PSPSCЦ PiPμPIPSPsPiPs, PiCfPsC,Pμ PSPμ CfC,P°C,PëCfC,PëC±PSPs P·PSP°C±CfC%oPsPiPs P·P±C-P»CHC€PμPSPSCЦ CfPëP·PëPeCf CfPSP·PIPëC,PeCf PIPμPSPsP·PSPsC— C,CfPSPjP±PsPμPjP±PsP»C-C— (C,CfPSPjP±PsP· PiP»PëP±PsPePëC... PIPμPS, C,CfPSPjP±PsPμPjP±PsP»C-CЦ P»PμPiPμPSPμPIPsC— P°CfC,PμCfC-C—), PiPsPIBf™ CЦP·P°PSPsPiPs C-P· P·P°CfC,PsCfCfPIP°PSPSCЦPj PiCfPμPiP°CfP°C,C-PI, C%oPs PjC-CfC,CЦC,CH C,C-P»CHPePë PiCfPSPiPμCfC,PsPiPμPS. P—P°PiP°P»CHPSPs PIPëP·PSP°PSC- C,,P°PeC,PsCfPë, C%oPs PiC-PrPIPëC%oCfCfC,CH CfPëP·PëPe PIPëPSPëPePSPμPSPSCЦ PIPμPSPsP·PSPsC— C,CfPSPjP±PsPμPjP±PsP»C-C— (P'PÿP•), PIPeP»CHC±P°CfC,CH: PsCfPsP±PëCfC,PëPNë P°P±Ps CfC-PjPμPNëPSPëPNë P°PSP°PjPSPμP· (PSP°PiCfPëPeP»P°Pr, PIPëPiP°PrPePë P'PÿP· Cr P±CfP°C,C-PI C±Pë CfPμCfC,PμCf P°P±Ps P±P°C,CHPeC-PI Cr PIC-PrPSPsCfPSPs PjPsP»PsPrPsPjCr PIC-C†C-), PIC-Pe, PsP¶PëCfC-PSPSCЦ, C,CfPëPIP°P»Cf C-PjPjPsP±C-P»C-P·P°C†C-Cf, CfP°PrPëPeP°P»CHPSC- C...C-CfCfCfPiC-C±PSC- PIC,CfCfCfP°PSPSCЦ P°P±Ps C,CfP°PIPjPë. Pj PIPëPiP°PrPeCf C,CfPëPIP°P»PsC— C-PjPjPsP±C-P»C-P·P°C†C-C— CfPμPePsPjPμPSPrCfC,C,CHCfCЦ PiCfPëPiPëPSPëC,Pë P·P°CfC,PsCfCfPIP°PSPSCЦ PiCfPμPiP°CfP°C,Cr CP°PIC-Cf (PiCfPë PiP»P°PSPsPIPëC... PsPiPμCfP°C†C-CЦC... C%oPsPSP°PNëPjPμPSC€Pμ P·P° 4 C,PëP¶PSC- PrPs C—C— PiCfPSPiPμPrPμPSPSCЦ) C- PSPμ PiPsC±PëPSP°C,Pë P·PSPsPICr PNëPsPiPs PiCfPëPNëPsPj CfP°PSC-C€Pμ PSC-P¶ C±PμCfPμP· 2 C,PëP¶PSC- PiC-CfP»CЦ PiPsPIPSPsC— CfPμPjPsP±C-P»C-P·P°C†C-C—.

PkPμPsP±C...C-PrPSPs P±CfP°C,Pë PrPs CrPIP°PiPë PiC-PrPIPëC%oPμPSPSCЦ CfPëP·PëPeCf CfPSP·PIPëC,PeCf C,CfPSPjP±PsPμPjP±PsP»C-C— Cr PiC-CfP»CЦPiPsP»PsPiPsPIPsPjCr PiPμCfC-PsPrC-.

Pj CfP°P·C- PIPëPSPëPePSPμPSPSCЦ CfPëPjPiC,PsPjC-PI PIPμPSPsP·PSPëC... C,P° P°CfC,PμCfC-P°P»CHPSPëC... C,CfPSPjP±PsC,PëC±PSPëC... P·P°C...PIPsCfCfPIP°PSCH P°P±Ps PiC-PrPsP·CfPë PSP° PSPëC... P»C-PeCfPIP°PSPSCЦ CfP»C-Pr PiCfPëPiPëPSPëC,Pë.

PμCfC...P»PëPSPë

РњРµС,Р°-Р°PSP°P»C-Р 54 РµРµС-РrРµРµС-РsP»PsPcC-C#PSPёC... РrPsCГP»C-РrP¶PµPSCН
PIPeP°P·CрC” PSP° PSPµP·PSP°C#PSPµ PиC-РrPIPёC%°PµPSPSCЦ PIC-РrPSPsCГPSPsPiPs
CГPёP·PёPeCр (P’P = 1,24) CГPсP·PIPёC,PeCр CГP°PeCр PjPsP»PsC#PSPsC— P·P°P»PsP·Pё Cр
P¶C-PSPsPe, CЦPeC- P·P°CГC,PsCГPсPICрCГC,CH PиPµCГPсCГP°P»CHPSC-
PePsPSC,CГP°C†PµPиC,PёPIPё (PµPµ), PiPsP»PsPIPSPёPj C#PёPSPsPj C,C-, C%°Ps
PjC-CГC,CЦC,CH PµCГC,CГPсPiPµPS-PиCГPсPiPµCГC,PsPiPµPS. PµPµP№
PиC-РrPIPёC%°PµPSPёP№ CГPёP·PёPe PиPsCГC,CрPиPsPIPс P·PSPёPeP°C” PиCГPсC,CЦPiPsPj 10
CГPсPeC-PI PиC-CГP»CЦ P·P°PeC-PSC#PµPSPSCЦ PиCГPёP№PsPjCр PePsPjP±C-PSPsPIP°PSPёC...
PиPµCГPсCГP°P»CHPSPёC... PePsPSC,CГP°C†PµPиC,PёPIC-PI (PµPµPµ). P¶CГPёC-Р»CHPePё
CГP°Pe PjPsP»PsC#PSPsC— P·P°P»PsP·Pё Cр P¶C-PSPsPe, PIC-PePsPj PrPs 40 CГPсPeC-PI
P·CрCГC,CГC-C#P°C”C,CHCГCЦ CГC-РrPePs, P·P±C-Р»CHCёPµPSPSCЦ PeC-Р»CHPePsCГC,C-
PIPёPиP°PrPeC-PI Prc-P°PiPSPsCГC,PёPePё CГP°PeCр PjPsP»PsC#PSPsC— P·P°P»PsP·Pё Cр
P¶C-PSPsPe, CЦPeC- PIPёPePsCГPёCГC,PsPICрCГC,CH P°P±Ps PSPµC%°PsPrcP°PIPSPs
PIPёPePsCГPёCГC,PsPICрPIP°P»Pё PµPµPµ, C” PSPµP·PSP°C#PSPёPj C%°PsPrcPs
P·P°PиP°P»CHPSPsPiPs CГPёP·PёPeCр CГP°PeCр PjPsP»PsC#PSPsC— P·P°P»PsP·Pё. P†CГPсCрC”
PsPrcPSP°PePsPIPёP№ CГPёP·PёPe PIPёCЦPIP»PµPSPSCЦ CГP°PeCр PjPsP»PsC#PSPsC—
P·P°P»PsP·Pё Cр P¶C-PSPsPe, CЦPeC- PиCГPёP№PjP°P»Pё PиCГPµPиP°CГP°C,Pё, C%°Ps
PjC-CГC,CЦC,CH C,C-Р»CHPePё PиCГPсPiPµCГC,PsPiPµPS, P°P±Ps PµPµPµ. P¶PrcPSP°Pe
C-PSC,,PsCГPjP°C†C-CЦ, C%°Ps CГC,PsCГCрC”C,CHCГCЦ PиCГPµPиP°CГP°C,C-PI, CЦPeC-
PjC-CГC,CЦC,CH C,C-Р»CHPePё PиCГPсPiPµCГC,PsPiPµPS, P±P°P·CрC”C,CHCГCЦ PSP°
PSP°P±P°PиP°C,Ps PjPµPSCёC-P№ PeC-Р»CHPePsCГC,C- P¶C-PSPsPe, CЦPeC- C—C...
P·P°CГC,PsCГPсPICрCГC,CH, C- C,PsPjCр PIPsPSP° C” PjPµPSCё PиPµCГPµPePsPSP»PёPIPsCГ,
PSC-Р¶ PrcP°PSC-, C%°Ps CГC,PsCГCрCГC,CHCГCЦ PµPµPµ. P PµP·CрP»CHC,Р°C,Pё C†PёC...
PrcPsCГP»C-РrP¶PµPSCН PSPµ PSP°PrcP°CГC,CH PrcPsPеP°P·C-PI C-CГPSCрPIP°PSPSCЦ
PиCГPёC#PёPSPSPsPiPs PIP·P°C”PjPsP·PиP¶™ CЦP·PeCр. PµC-РrPIPёC%°PµPSPSCЦ CГPёP·PёPeCр
PjPsP¶Pµ P±CрC,Pё P·CрPjPsPIP»PµPSPµ CЦPe P±C-Р»CHCё CГP°PSPSCHPсCГ
Prc-P°PiPSPsCГC,PёPePsCГ CГP°PeCр PjPsP»PsC#PSPsC— P·P°P»PsP·Pё Cр P¶C-PSPsPe, CЦPeC-
P·P°CГC,PsCГPсPICрCГC,CH PµPµ, C,P°Pe C- P±C-PsP»PsPиC-C#PSPsCГ Prc-C”CГ C†PёC...
PиCГPµPиP°CГP°C,C-PI, P°P±Ps PиPsC”PrcPSP°PSPSCЦPj PsP±PsC... C,,P°PeC,PsCГC-PI.
P’C-РrP·PSP°C#PµPSPs C,PµPSPrcPµPSC†C-CГ, C%°Ps CГP°Pe PjPsP»PsC#PSPsC— P·P°P»PsP·Pё,
PIPёCЦPIP»PµPSPёP№ Cр P¶C-PSPsPe, CЦPeC- PePsP»Pё-PSPµP±CрPrc PиCГPёP№PjP°P»Pё
PµPµ, PeP»C-PSC-C#PSPs PjPµPSCё PIPёCГP°P¶PµPSPёP№, PSC-Р¶ Cр C,PёC..., C...C,Ps
PSC-PePsP»Pё PSPµ P·P°CГC,PsCГPсPICрPIP°PI PµPµ.

Pj PиPsPsPrcPёPSPsPePёC... PIPёPиP°PrcPеP°C... Cр P¶C-PSPsPe, CЦPeC-
P·P°CГC,PsCГPсPICрPIP°P»Pё PиPsCГPjPsPSP°P»CHPSC- CГPµC#PsPIPёPSPё, PиPsPrc-P±PSC-
PrcPs C,C-C”C—, C%°Ps PjC-CГC,PёC,CH PиCГPµPиP°CГP°C, P’P°PIC-CГ,
CГPиPsCГC,PµCГC-PиP°P»PёCГCЦ PrcPsP±CГPсCЦPeC-CГPSC-, P° C%°Pµ CГC-РrcPµ P¶”
P·P»PsCЦPeC-CГPSC- PиCрC...P»PёPSPё PиPµC#C-PSPePё, CЦPeC- PI PsPeCГPµPjPёC...
PIPёPиP°PrcPеP°C... PиCГPёP·PIPсPrcPёP»Pё PrcPs PSPµP±PµP·PиPµC#PSPsC— PrcP»CЦ P¶PёC,C,CЦ
PIPSCрC,CГC-CёPSCНPsC#PµCГPµPIPSPsC— PeCГPсPIPсC,PµC#C-. Pj PIPёPиP°PrcPеCр
PIPёPSPёPePSPµPSPSCЦ CГPеP°CГPи PSP° CГPёP»CHPSPёP№ P±C-Р»CH PI
PµPиC-PиP°CГC,CГP°P»CHPSC-P№ Prc-Р»CЦPSC†C-, P·P±C-Р»CHCёPµPSPSCЦ
PиPµC#C-PSPePё P°P±Ps PиPsCЦPIPё PsP·PSP°Pe PIPSCрC,CГC-CёPSCНPsC#PµCГPµPIPSPsC—
PeCГPсPIPсC,PµC#C- PиCГPё PrcPёC,,PµCГPµPSC†C-P№PSC-P№ Prc-P°PiPSPsCГC,PёC†C-
CГP»C-Рr PICГP°C...PsPICрPIP°C,Pё PjPsP¶P»PёPIC-CГC,CH PSP°CЦPIPsCГC,C-
PиCрC...P»PёPSPё PиPµC#C-PSPePё Cр P¶C-PSPsPe, CЦPeC- PиCГPёP№PjP°CГC,CH
Prc-C”PSPsPiPµCГC,, C,P°P±P»PµC,PePё PиPs 2 PjPi.

P¶CГC,PµPsPiPsCГPсP·

P—PjC—PSPë PjC—PSPµCḡP°P»CH̄PSPsC— C%oC—P»CH̄PSPsCḡC,C- PeC—CḡC,PePsPIPsC— C,PeP°PSPëPSPë (PḡP©PḡPḡ).

P—P°CḡC,PsCḡCḡPIP°PSPSCḡ PrC—C”PSPsPiPµCḡC,Cḡ, C,P°P±P»PµC,PsPe 2 PjPi, PiC—PrP»C—C,PeP°Pj (12 Bḡ“ <18 CḡPsPeC—PI) PiCḡPsC,CḡPiPsPj PiPµCḡC—PsPrCḡ P»C—PeCḡPIP°PSPSCḡ 12 PjC—CḡCḡCḡC—PI P°CḡPsCḡC—CḡPIP°P»PsCḡCḡ P·C— P·PSPëPḡPµPSPSCḡPj CḡPµCḡPµPrPSCḡPsPiPs P·PSP°CḡPµPSPSCḡ PḡP©PḡPḡ Cḡ PiPsPiPµCḡPµPePsPIPsPjCḡ PIC—PrPrC—P»C— C...CḡPµP±C,P° (L2 Bḡ“ L4). PḡPµCḡPµPrPSCḡ PIC—PrPSPsCḡPSP° P·PjC—PSP° PḡP©PḡPḡ PIC—Pr PIPëC...C—PrPSPëC... PiPsPeP°P·PSPëPeC—PI PrPs P·P°PeC—PSCḡPµPSPSCḡ P»C—PeCḡPIP°PSPSCḡ CḡC,P°PSPsPIPëP»P° — 1,2 % P· PrC—P°PiP°P·PsPSPsPj PjC—Pḡ Bḡ“6 % C,P° 5 % (P”Pḡ 95 %: Bḡ“1,70 % C,P° Bḡ“0,78 %, n=103).

PµPsPIC,PsCḡPSPµ PIPëPjC—CḡCḡPIP°PSPSCḡ CḡPµCḡPµP· 6 PjC—CḡCḡCḡC—PI PiC—CḡP»Cḡ P·P°PeC—PSCḡPµPSPSCḡ P»C—PeCḡPIP°PSPSCḡ Cḡ PiC—PrPiCḡCḡPiC— P·C— P·PSPëPḡPµPSPëPjPë P·PSP°CḡPµPSPSCḡPjPë PḡP©PḡPḡ PiPsPeP°P·P°P»Ps C,PµPSPPrPµPSCḡC—Cḡ PrPs PIC—PrPSPsPIP»PµPSPSCḡ (CḡPµCḡPµPrPSCḡ PIC—PrPSPsCḡPSP° P·PjC—PSP° PIC—Pr PIPëC...C—PrPSPëC... PiPsPeP°P·PSPëPeC—PI: Bḡ“2,3 % PiCḡPë P·P°PeC—PSCḡPµPSPSC— P»C—PeCḡPIP°PSPSCḡ C,P° Bḡ“0,6 % CḡPµCḡPµP· 6 PjC—CḡCḡCḡC—PI PiC—CḡP»Cḡ P·P°PeC—PSCḡPµPSPSCḡ P»C—PeCḡPIP°PSPSCḡ P· PrC—P°PiP°P·PsPSPsPj PjC—Pḡ Bḡ“9 % C,P° 6 % (P”Pḡ 95 %: Bḡ“1,20 % C,P° 0,06 % (n=60)).

PµPsCḡCḡCḡPµPSPSCḡ PḡP©PḡPḡ PjP°C” PsCḡPsP±P»PëPIPµ P·PSP°CḡPµPSPSCḡ Cḡ PiC—PrP»C—C,PePsPIPsPjCḡ PIC—CḡC— C,P° Cḡ CḡP°PSPSC—Pḡ PiPµCḡC—PsPr CḡC,P°C,PµPIPsPiPs PrPsP·CḡC—PIP°PSPSCḡ, PeCḡPëC,PëCḡPSPëPḡ PiPµCḡC—PsPr CḡPsCḡC,Cḡ PeC—CḡC,PsPe. PḡPµPIC—PrPsPjPs, CḡPë P·PjPµPSCḡPëC,CH̄ PiC—PePsPICḡ PeC—CḡC,PePsPICḡ PjP°CḡCḡ C,P° PiC—PrPIPëC%oPëC,CH̄ CḡPëP·PëPe PiPµCḡPµP»PsPjCḡ PeC—CḡC,PsPe Cḡ P»C—C,PSCḡPsPjCḡ PIC—CḡC— P·PSPëPḡPµPSPSCḡ PḡP©PḡPḡ Cḡ CḡC—Pḡ PiPsPiCḡP»CḡCḡC— (PrPëPI. CḡPsP·PrC—P»Pë B«PḡP°CḡPjP°PePsP»PsPiC—CḡPSC— PIP»P°CḡC,PëPIPsCḡC,C—B» C,P° B«P”C—C,PëB»).

Pj PiP°CḡC—C”PSC,PsPe, CḡPeC— P·PSP°C...PsPrCḡC,CH̄CḡCḡ Cḡ PiCḡCḡPiC— PiC—PrPIPëC%oPµPSPsPiPs CḡPëP·PëPeCḡ CḡPsP·PIPëC,PeCḡ PsCḡC,PµPsPiPsCḡPsP·Cḡ, CḡPµC,PµP»CH̄PSP° PsCḡC—PSPeP° CḡPiC—PIPIC—PrPSPsCḡPµPSPSCḡ CḡPëP·PëPe/PePsCḡPëCḡC,CH̄ PiPsPIPëPSPSP° P±CḡC,Pë PiCḡPsPIPµPrPµPSP° PrPs PiPsCḡP°C,PeCḡ P»C—PeCḡPIP°PSPSCḡ PiCḡPµPiP°CḡP°C,PsPj PḡP°PIC—Cḡ, PsCḡPeC—P»CH̄PePë CḡC—PIPµPSCḡ PµPSPPrPsPiPµPSPSPëC... PµCḡC,CḡPsPiPµPSC—PI PiPsPjC—CḡPSPs P·PSPëPḡCḡC,CH̄CḡCḡ PSP° C,P»C— P»C—PeCḡPIP°PSPSCḡ PiCḡPµPiP°CḡP°C,PsPj PḡP°PIC—Cḡ (PrPëPI. CḡPsP·PrC—P» B«PḡP°CḡPjP°PePsPrPëPSP°PjC—PeP°B»).

PµPµCḡPµPr PiPsCḡP°C,PePsPj P»C—PeCḡPIP°PSPSCḡ P»C—PeP°CḡCḡ CḡP»C—Pr P·PIP°PḡPëC,Pë PiPµCḡPµPIP°PiPë P·P°CḡC,PsCḡCḡPIP°PSPSCḡ PiCḡPµPiP°CḡP°C,Cḡ PḡP°PIC—Cḡ C,P° PjPsPḡP»PëPIC— CḡPëP·PëPePë P·P°CḡC,PsCḡCḡPIP°PSPSCḡ PḡPsPiPs PrP»Cḡ PePsPḡPSPsPiPs PsPeCḡPµPjPsPiPs PiC—PrP»C—C,PeP°, PICḡP°C...PsPICḡCḡCḡPë C,P°PePsPḡ PSP°CḡPIPSC—CḡC,CH̄ CḡCḡC,C,C”PIPëC... C,,P°PeC,PsCḡC—PI CḡPëP·PëPeCḡ PsCḡC,PµPsPiPsCḡPsP·Cḡ.

PḡPrPµPePIP°C,PSPµ P·P°CḡC,PsCḡCḡPIP°PSPSCḡ PeP°P»CH̄CḡC—Cḡ C,P° PIC—C,P°PjC—PSCḡ D PiCḡPë PrC—C”C,PëCḡPSPsPjCḡ C...P°CḡCḡCḡPIP°PSPSC— P°P±Ps PiCḡPë P·P°CḡC,PsCḡCḡPIP°PSPSC— C...P°CḡCḡPsPIPëC... PrPsP±P°PIPsPe C” PIP°PḡP»PëPIPëPj PrP»Cḡ P·PrPsCḡPsPIPsPiPs CḡC,P°PSCḡ PeC—CḡC,PePsPIPsC— C,PeP°PSPëPSPë Cḡ PḡC—PSPsPe CḡCḡC—C... PIC—PePsPIPëC... PeP°C,PµPiPsCḡC—C—.

СГСГРiСГПsPIPsPrP¶CГPIP°С,РёСГСЦ P±PsP»PµPj СГ PrC-P»CЦPSC†C- C,P°P·P°.

РкPµ P·P°СГС,PsСГPsPICrСГС,СГ СГ PiPµСГС-P°С,СГPёC±PSC-PNё PiСГP°PeC,РёC†C-.

P»P°PeC,PsP·P°

PhPrPSP° C,P°P±P»PµC,PeP° PiСГPµPiP°СГP°С,СГ PŸP°PIC-СГ PjC-СГС,РёC,СГ 62,8 PjPi P»P°PeC,PsP·Pё PjPsPSPsPiC-PrСГP°С,СГ. PµP°C†C-C”PSC,P°Pj P· СГС-PrPeC-СГPSPёPjPё СГPiP°PrPePsPIPёPjPё P·P°С...PIPsСГСГPIP°PSPSCЦPjPё, PiPsPIBГ™ CЦP·P°PSPёPjPё P· PSPµPiPµСГPµPSPsСГPёPjC-СГС,СГ PiP°P»P°PeC,PsP·Pё, PiPsPIPsСГ P»P°PeC,P°P·PSPsСГ PSPµPrPsСГС,P°С,PSC-СГС,СГ P°P±Ps PjP°P»СГP°P±СГPsСГP±C†C-C”СГ PiP»СГPePsP·Pё- PiP°P»P°PeC,PsP·Pё, PSPµ СГP»C-Pr PiСГPёPNёPjP°С,РёB C†PµPNё P»C-PeP°СГСГСГPёPNё P·P°СГС-P±.

P—P°СГС,PsСГСзPIP°PSPSCЦ Сз PiPµСГС-PsPr PIP°PiC-C,PSPsСГС,C- P°P±Ps PiPsPrCзPIP°PSPSCЦ PiСГСзPrPrСГ.

P°P°PiC-C,PSC-СГС,СГ

P†СГPSCrСГС,СГ PsP±PjPµP¶PµPSC- PrP°PSC- C%PsPrPs P·P°СГС,PsСГСГPIP°PSPSCЦ PrC-C”PSPsPiPµСГС,СГ PIP°PiC-C,PSPёPj P¶C-PSPeP°Pj. P”PsСГP»C-PrP¶PµPSPSCЦ PSP° C,PIP°СГPёPSP°С... PSPµ PIPeP°P·CГСГС,СГ PSP° PiСГСЦPjPёPNё P°P±Ps PSPµPiСГСЦPjPёPNё СГPёP·PёPePё СГPµPiСГPµPrCГPeC,РёPIPsC— C,PsPeСГPёC±PSPsСГС,C- (PrPёPi. СГPµP·PrC-P» B«PαP°СГPjP°PePsP»PsPiC-C±PSC- PIP»P°СГС,РёPIPsСГС,C-B»).

PŸP°PIC-СГ PSPµ СГPµPePsPjPµPSPPrCГC,СГСГСЦ P·P°СГС,PsСГPsPICrPIP°С,Рё PIP°PiC-C,PSPёPj P¶C-PSPeP°Pj, C,PsPjCГ C%Ps PSPµPjP°С” PiPsC,СГPµP±Pё P»C-PeCГPIP°С,Рё PµPSPPrPsPjPµC,СГС-PsP· СГ PiPµСГС-PsPr PIP°PiC-C,PSPsСГС,C-.

PµPµСГС-PsPr PiPsPrCГPIP°PSPSCЦ PiСГСГPrPrСГ

P»C-PeCГPIP°PSPSCЦ PiСГPµPiP°СГP°С,PsPj PŸP°PIC-СГ СГ PiPµСГС-PsPr PiPsPrCГPIP°PSPSCЦ PiСГСГPrPrСГ PSPµ СГPµPePsPjPµPSPPrCГC,СГСГСЦ.

РкPµPIC-PrPsPjPs, C±Pё PiСГPµPSPёPeP°С” PrC-C”PSPsPiPµСГС, СГ PiСГСГPrPSPµ PjPsP»PsPePs P¶C-PSPePё. P”P°PSC-, PsC,СГPёPjP°PSC- СГ PiСГPµC†PµСГС- PrPsСГP»C-PrP¶PµPSCСГ PSP° C,PIP°СГPёPSP°С..., PIPeP°P·CГСГС,СГ PSP° PiСГPµPSPёPePSPµPSPSCЦ PrC-C”PSPsPiPµСГС,СГ СГ PiСГСГPrPSPµ PjPsP»PsPePs C%СГСГС-PI.

PŸP»C-Pr PiСГPёPNёPSCЦ,Рё СГС-CёPµPSPSCЦ PiСГPµ PiСГPёPiPёPSPµPSPSCЦ PiPsPrCГPIP°PSPSCЦ PiСГСГPrPrСГ P°P±Ps PiСГPёPiPёPSPµPSPSCЦ C,PµСГP°PiC-C— PiСГPµPiP°СГP°С,PsPj PŸP°PIC-СГ, PICГP°С...PsPICrСГС±Pё B PePsСГPёСГС,СГ PiPsPrCГPIP°PSPSCЦ PiСГСГPrPrСГ PrP»CЦ PrPёC,РёPSPё C- PSPµPsP±C...C-PrPSC-СГС,СГ C,PµСГP°PiC-C— PrP»CЦ P¶C-PSPePё.

PαPµСГС,РёP»СГPSC-СГС,СГ

РкP° PiC-PrСГС,P°PIC- PSP°CЦPIPsPёC... PrP°PSPёC... PjPsP¶PSP° СГС,PIPµСГPµP¶CГPIP°С,Рё, C%Ps PiC-Pr C±P°СГ P»C-PeCГPIP°PSPSCЦ PiСГPµPiP°СГP°С,PsPj PŸP°PIC-СГ СГ P±C-P»СГСёPsСГС,C- PiP°C†C-C”PSC,PsPe C-PSPiC-P±CГC,СГСГСЦ PsPICrP»CЦC†C-CЦ. PhPrPSP°Pe PiСГPµPiP°СГP°С, PŸP°PIC-СГ PSPµ C” PiСГPµC,РёP·P°PiP»C-PrPSPёPj

P·P°CÍPsP±PsPj.

PİPeC%oPs PİPsC,CTHC-P±PSP° PePsPSC,CTHP°C†PµPİC†C-Cİ, CÍP»C-Pr PrPsPrP°C,PePsPIPs
P·P°CÍC,PsCÍPsPICrPIP°C,Pë PSPµPİPsCTHPjPsPSP°P»CHBPSPëPNë PjPµC,PsPr
P·P°PİPsP±C-PİP°PSPSCİ PIP°PİC-C,PSPsCÍC,C- (PrPëPI. CTHPsP·PrC-P» B«PÿPİPsCÍC-P±
P·P°CÍC,PsCÍCfPIP°PSPSCİ C,P° PrPsP·PëB»).

PkP° PİC-PrCÍC,P°PIC- PSP°CİPIPSPëC... PrP°PSPëC... PjPsP¶PSP° CÍC,PIPµCTHPPrP¶CfPIP°C,Pë,
C%oPs PjPµPSCÍC,CTHCfP°P»CHBPSPëPNë C†PëPeP» PİPsPIPµCTHC,P°C”C,CHCÍCİ PrPs
PSPsCTHPjPë PİCTHPsC,CİPİPsPj 2 PjC-CÍCİC†C-PI PİC-CÍP»Cİ PİCTHPëPİPëPSPµPSPSCİ
P»C-PeCfPIP°PSPSCİ PrC-C”PSPsPİPµCÍC,PsPj, C,P°P±P»PµC,PeP°PjPë 2 PjPi.

P—PrP°C,PSC-CÍC,CH PIPİP»PëPIP°C,Pë PSP° C€PIPëPrPeC-CÍC,CH CTHPµP°PeC†C-C— PİCTHPë
PePµCTHCzPIP°PSPSC- P°PIC,PsC,CTHP°PSCÍPİPsCTHC,PsPj P°P±Ps C-PSC€PëPjPë
PjPµC...P°PSC-P·PjP°PjPë. PkPµ CÍPİPsCÍC,PµCTHC-PİP°P»Pë PIPİP»PëPICr PSP°
P·PrP°C,PSC-CÍC,CH PePµCTHCfPIP°C,Pë P°PIC,PsC,CTHP°PSCÍPİPsCTHC,PsPj C,P°
CfPİCTHP°PIP»CİC,Pë PjPµC...P°PSC-P·PjP°PjPë CÍ PİP°C†C-C”PSC,PsPe, CİPeC-
PİCTHPëPNëPjP°P»Pë PİCTHPµPİP°CTHP°C,Pë, C%oPs PjC-CÍC,CİC,CH PrC-C”PSPsPİPµCÍC,.

PÿPİPsCÍC-P± P·P°CÍC,PsCÍCzPIP°PSPSCİ C,P° PrPsP·Pë.

PÿPİPsCÍC-P± P·P°CÍC,PsCÍCzPIP°PSPSCİ

P”P»Cİ PİPµCTHPsCTHP°P»CHBPSPsPİPs P·P°CÍC,PsCÍCfPIP°PSPSCİ.

P”PsP·CzPIP°PSPSCİ

PµCTHPëPNëPjP°C,Pë PİPs 1 C,P°P±P»PµC,C†C- C%oPsPrPSCİ P±PµP· PİPµCTHPµCTHIPİPë CÍ
P·P°CÍC,PsCÍCfPIP°PSPSC- PİCTHPµPİP°CTHP°C,CÍ PİCTHPëP±P»PëP·PSPs Pİ PsPrPëPS C- C,PsPNë
P¶Pµ C†P°CÍ, PİCTHPë PSPµPsP±C...C-PrPSPsCÍC,C- P·P°PİPëPIP°CTHC†Pë PSPµPIPµP»PëPePsCTH
PeC-P»CHPeC-CÍC,CTH CTHC-PrPëPSPë. PÿP°P±P»PµC,PePë PjPsP¶PSP° PİCTHPëPNëPjP°C,Pë
PSPµP·P°P»PµP¶PSPs PIC-Pr PIP¶PëPIP°PSPSCİ C—P¶C-.

PÿP°P±P»PµC,PePë CÍP»C-Pr PİCTHPëPNëPjP°C,Pë CTHPµPİCfP»CİCTHPSPs, PSPµP·P°P»PµP¶PSPs
PIC-Pr PjPµPSCÍC,CTHCfP°P»CHBPSPsC— PeCTHPsPIPsC,PµC†C-. PİPe C,C-P»CHPePë
C,P°P±P»PµC,PePë P· PsPrPSC-C”C— CÍPİP°PePsPIPePë P·P°PeC-PSC†P°C,CHCÍCİ,
PSPµPsP±C...C-PrPSPs PİPsC†PëPSP°C,Pë PİCTHPëPNëPjP°C,Pë C,P°P±P»PµC,PePë P·
PSP°CÍC,CfPİPSPsC— CÍPİP°PePsPIPePë, PSPµ CTHPsP±P»CİC†Pë PİPµCTHPµCTHIPİPë CÍ
P·P°CÍC,PsCÍCfPIP°PSPSC- P»C-PeP°CTHCÍCHPePsPİPs P·P°CÍPsP±CÍ.

PµCTHPëPNëPsPj PİCTHPµPİP°CTHP°C,CÍ PjPsP¶PSP° CTHPsP·PİPsC†P°C,Pë CÍ P±CÍPrCHC-CİPePëPNë
PrPµPSCH PjPµPSCÍC,CTHCfP°P»CHBPSPsPİPs C†PëPeP»CÍ.

P—P°CÍC,PsCÍCfPIP°PSPSCİ P±CÍPrCHC-CİPePëC... PİPsCTHPjPsPSP°P»CHBPSPëC...
PePsPSC,CTHP°C†PµPİC,PëPIC-PI CÍP»C-Pr PİCTHPëPİPëPSPëC,Pë PİPµCTHPµPr PİPsC†P°C,PePsPj
C,PµCTHP°PİC— PİCTHPµPİP°CTHP°C,PsPj PÿP°PIC-CÍ. PİPeC%oPs PSPµPsP±C...C-PrPSP°
PePsPSC,CTHP°C†PµPİC†C-Cİ, CÍP»C-Pr P·P°CÍC,PsCÍPsPICrPIP°C,Pë
PSPµPİPsCTHPjPsPSP°P»CHBPSPëPNë PjPµC,PsPr P·P°PİPsP±C-PİP°PSPSCİ PIP°PİC-C,PSPsCÍC,C-
(PSP°PİCTHPëPeP»P°Pr, P±P°CTHBTM C”CTHPSPëPNë PjPµC,PsPr).

РиЧѣPsPiCfCfPe PiCѣPēPNēPsPjCf C, P°P±P»PμC,PsPe

PJ PIPēPiP°PrPeCf PiCѣPsPiCfCfPeCf PiCѣPēPNēPsPjCf C, P°P±P»PμC,PsPe, P±P»CѢPIP°PSPSCII
C, P°/P°P±Ps PrC-P°CѢPμC— (CIIPeC- PjP°P»Pē PjC-CfCfPμ PiCѣPsC, CIIPIPsPj
3-4 PiPsPrPēPS PiC-CfP»CII PiCѣPēPNēPsPjCf C, P°P±P»PμC,PePē), PμC,,PμPeC,PēPIPSC-CfC,CH
PiCѣPμPiP°CѢP°C,Cf PŸP°PIC-Cf PjPsP¶Pμ P·PjPμPSCεPēC,PēCfCII. PJ CѢP°P·C-
PiCѣPsPiCfCfPeCf PiCѣPēPNēPsPjCf PsPrPSC-C”C— P°P±Ps PeC-P»CѢPePsC...
C, P°P±P»PμC,PsPe, CfP»C-Pr PiCѣPēPNēPSCII,C,Pē PsPrPSCf C, P°P±P»PμC,PeCf, CIIPe
C,C-P»CѢPePē P¶C-PSPeP° P·PiP°PrP°C” PiCѣPs CfPμ, P° PSP°CfC,CfPiPSCf PiCѣPēPNēPjP°C,Pē
Cf P·PIPēC±PSPēPNē C±P°Cf. PѣPSP°P»PsPiC-C±PSPs, C, P°P±P»PμC,PeCf, C°Ps PSPμ
PICfPjPsPeC, P°P»P°CfCII C±PμCѢPμP· P±P»CѢPIP°PSPSCII P°P±Ps PrC-P°CѢPμCѢ, CfP»C-Pr
P·P°PjC-PSPēC,Pē PSP° C-PSCεCf C, P°P±P»PμC,PeCf.

P—P°CfC,PsCfCfPIP°PSPSCII Cf PsCfPsP±P»PēPIPēC... PiCѣCfPiP°C... PiP°CfC-C”PSC,C-PI

PμP°CfC-C”PSC,Pē P»C-C,PSCHPsPiPs PIC-PeCf

PkPμPjP°C” PIC-PrPiPsPIC-PrPSPēC... PiPsPeP°P·P°PSCѢ PrP»CII P·P°CfC,PsCfCfPIP°PSPSCII
PiCѣPμPiP°CѢP°C,Cf PŸP°PIC-Cf PiP°CfC-C”PSC,PeP°Pj CfC-C”C— PiCѣCfPiPē.

PμPμC±C-PSPePsPIP° PSPμPrPsCfC,P°C,PSC-CfC,CH

PμCѢPμPiP°CѢP°C, PiCѣPsC,PēPiPsPeP°P·P°PSPēPNē PiP°CfC-C”PSC,PeP°Pj C-P· C,CII¶PePēPj
P·P°C...PIPSCѢCѢPIP°PSPSCII Pj PiPμC±C-PSPePē PSPēPSC- P°P±Ps PI P°PSP°PjPSPμP·C-
(PrPēPI. CѢPsP·PrC-P» B«PμCѢPsC,PēPiPsPeP°P·P°PSPSCII B»).

PkPēCѢPePsPIP° PSPμPrPsCfC,P°C,PSC-CfC,CH

PkPμPjP°C” P¶PsPrPSPēC... PrP°PSPēC..., C°Ps CfPIC-PrC±P°C,CH PiCѣPs PiPsC,CѢPμP±Cf PI
PePsCѢPμPeCfC-C— PrPsP·Pē PrP»CII PiP°CfC-C”PSC,PsPe P· PSPēCѢPePsPIPSCѢ
PSPμPrPsCfC,P°C,PSC-CfC,CѢ.

P”C-C,Pē.

PμCѢPμPiP°CѢP°C, PŸP°PIC-Cf PSPμ PiPsPeP°P·P°PSPēPNē PrP»CII P·P°CfC,PsCfCfPIP°PSPSCII
PrC-C,CII Pj PrPs PSP°CfC,P°PSPSCII PjPμPSP°CѢC...Pμ.

P’PμP·PiPμPeCf C,P° PμC,,PμPeC,PēPIPSC-CfC,CH P·P°CfC,PsCfCfPIP°PSPSCII
PrC-C”PSPsPiPμCfC,Cf, C, P°P±P»PμC,PsPe 2 PjPi, P±CfP»Ps PrPsCfP»C-PrP¶PμPSPs Cf
PiCѣPsCfPμCfC- PSPμPePsPSC,CѢPsP»CѢPsPIP°PSPsPiPs PrPsCfP»C-PrP¶PμPSPSCII
PiCѣPsC,CIIPIPsPj 12 PjC-CfCII CfC-PI Cf 111 PiP°CfC-C”PSC,PsPe PiC-PrP»C-C,PePsPIPμPiPs
PIC-PeCf (12 Bѣ” <18 CѢPsPeC-PI) P· PeP»C-PSC-C±PSPs PiC-PrPsP·CѢCѢPIP°PSPēPj P°P±Ps
PiC-PrC,PIPμCѢPrP¶PμPSPēPj PμPSPPrPsPjPμC,CѢC-PsP·PsPj (PrPēPI. CѢPsP·PrC-P»Pē
B«P°P°CѢPjP°PePsP»PsPiC-C±PSC- PIP»P°CfC,PēPIPsCfC,C-B» C,P°
B«PħCfPsP±P»PēPIPsCfC,C- P·P°CfC,PsCfCfPIP°PSPSCII B»).

PμPμCѢPμPrPsP·C±PIP°PSPSCII. P”PsCfP»C-PrP¶PμPSPSCII PiPsCfC,CѢPsC—
C,PsPeCfPēC±PSPsCfC,C-, PiCѣPsPIPμPrPμPSC- P· PrC-C”PSPsPiPμCfC,PsPj, PSPμ
PIPeP°P·CfPIP°P»Pē PSP° CѢPēP·PēPe CѢPsP·PIPēC,PeCf PiPsCfC,CѢPēC... PiPsP±C-C±PSPēC...

СҗРµP°PеC†C-PM₆ Cᵣ PIPëPİP°PrPеCᵣ PSpµPSP°PIPjPëCГPSPsPiPs PİCҗPëPN₆PsPjCᵣ
PеC-P»CHPеPsC... PrPsP±PsPIPëC... C, PµCҗP°PİPµPIC, PëC±PSPëC... PrPsP·. P-PsPrPSPëC...
CГPİPµC†PëC,,C-C±PSPëC... P°PSC,PëPrPsC,C-PI PSpµ C-CГPSCᵣC”.
P—P°CГC,PsCГCᵣPIP°PSPSCҘ 20-30 PjPi PrC-C”PSPsPiPµCГC,Cᵣ PSP° PrPsP±Cᵣ (C%Ps Cᵣ 10-15
CҗP°P·C-PI PIPëC%Ps, PSC-P¶ PrPsP·P° PI C,P°P±P»PµC,C†C- PİCҗPµPİP°CҗP°C,Cᵣ CP°PIC-CГ)
CᵣPİCҗPsPrPsPIP¶ P±C-P»CHC€Pµ 24 C,PëP¶PSC-PI PİPµCҗPµPSPsCГPëP»PsCГCҘ PrCᵣP¶Pµ
PrPsP±CҗPµ.

PµPsP±C-C±PSC- CҗPµP°PеC†C-C—.

PµPsP±C-C±PSC- CҗPµP°PеC†C-C— PsPİPëCГP°PSPs P·PİC-PrPSPs P· MedDRA.

PµPsP±C-C±PSC- CҗPµP°PеC†C-C— PSP°PN₆C±P°CГC,C-C€Pµ CҗPsP·PIPëPIP°CҗC,CHCГCҘ
PİCҗPsC,CҘPİPsPj PİPµCҗC€PëC... PjC-CГCҘC†C-PI P·P°CГC,PsCГCᵣPIP°PSPSCҘ
PİCҗPµPİP°CҗP°C,Cᵣ C- P·PSPëPеP°CҗC,CH Cᵣ PİCҗPsC†PµCГC- P»C-PeCᵣPIP°PSPSCҘ.
PҗPsP¶CᵣC,CH CГPİPsCГC,PµCҗC-PİP°C,PëCГCҘ P·PjC-PSPë C...P°CҗP°PеC,PµCҗCᵣ
PеCҗPsPIPсC,PµC±, C,P°PеC- CҘPе PеCҗPsPIPсPjP°P·P°PSPSCҘ, PSpµCҗPµPİCᵣP»CҘCҗPSC-
PеCҗPsPIPсC,PµC±C- P°P±Ps P°PjPµPSPsCҗPµCҘ.

PµPsPIC-PrPsPjP»CҘP»PsCГCҘ PİCҗPs PSPëP¶C±PµP·P°P·PSP°C±PµPSC- PİPsP±C-C±PSC-
CҗPµP°PеC†C-C— PİC-Pr C±P°CГ P»C-PeCᵣPIP°PSPSCҘ PrC-C”PSPsPiPµCГC,PsPj,
C,P°P±P»PµC,PeP°PjPë 2 PjPi. PµPsP±C-C±PSC- CҘPIPëC%Ps, PİCҗPs CҘPеC-
PSP°PN₆C±P°CГC,C-C€Pµ PİPsPIC-PrPsPjP»CҘP»Pë PİC-Pr C±P°CГ P·P°CГC,PsCГCᵣPIP°PSPSCҘ
PİCҗPµPİP°CҗP°C,Cᵣ, PİPеP»CҗC±P°P»Pë PİPsP»PsPIPSPëPN₆ P±C-P»CH (9,0 %),
PrPëCГPеPsPjC,,PsCҗC, Cᵣ PjPsP»PsC±PSPëC... P·P°P»PsP·P°C... (5,4 %),
PİCҗPëPİPSC-C±PµPSPëPN₆ PSP°CГC,CҗC-PN₆ (5,1 %) C,P° P°PеPSPµ (5,1 %).

PҗCҗC-Pj C,PsPiPs, P·P°CГC,PsCГCᵣPIP°PSPSCҘ PİCҗPµPİP°CҗP°C,Cᵣ PIPİP»PëPIP°C” PSP°
C...P°CҗP°PеC,PµCҗ PjPµPSCГC,CҗCᵣP°P»CHPSPëC... PеCҗPsPIPсC,PµC± Cᵣ
P±C-P»CHC€PsCГC,C- P¶C-PSPsPе. PГP°CҗP°PеC,PµCҗ PjPµPSCГC,CҗCᵣP°P»CHPSPëC...
PеCҗPsPIPсC,PµC± PsC†C-PSCҗPİP°P»Pë CГPëCГC,PµPjP°C,PëC±PSPs P·
PIPëPеPsCҗPëCГC,P°PSPSCҘPj C%PsPrPµPSPSPëPеC-PI PİP°C†C-C”PSC,PsPе C,P°
P°PSP°P»C-P·CᵣPIP°P»Pë C-P· P·P°CГC,PsCГCᵣPIP°PSPSCҘPj PjPµC,PsPrCᵣ P’PhPhP—
PİCҗPsC,CҘPİPsPj 90-PrPµPSPSPsPiPs P·PIC-C,PSPsPiPs PİPµCҗC-PsPrCᵣ. PµCҗPsC,CҘPİPsPj
PİPµCҗC€PëC... 90 PrPSC-PI C,PµCҗP°PİC-C— PrC-C”PSPsPiPµCГC,PsPj, C,P°P±P»PµC,PeP°PjPë
2 PjPi, CГPİPsCГC,PµCҗC-PİP°P»Pë C,P°PеC- B PеCҗPsPIPсC,PµC±C- P·P°
C...P°CҗP°PеC,PµCҗPsPj B (n=290; 100 %): P°PjPµPSPsCҗPµCҘ (1,7 %), PSpµC±P°CГC,C-
PеCҗPsPIPсC,PµC±C- (27,2 %), C±P°CГC,C- PеCҗPsPIPсC,PµC±C- (13,4 %),
PSPµCҗPµPİCᵣP»CҘCҗPSC- PеCҗPsPIPсC,PµC±C- (35,2 %), C,CҗPëPIP°P»C-
PеCҗPsPIPсC,PµC±C- (38,3 %), PSPsCҗPjP°P»CHPSP° PjPµPSCГC,CҗCᵣP°P»CHPSP°
PеCҗPsPIPсC,PµC±P°, C,PsP±C,Ps C,P°PеP° C%Ps PSpµ PSP°P»PµP¶PëC,CH PrPs
B P¶PsPrPSPсC— B C-P· PİPsPİPµCҗPµPrPSC-C... PеP°C,PµPİPsCҗC-PN₆ (19,7 %).
PµCҗPsC,CҘPİPsPj C±PµC,PİPµCҗC,PsPiPs P·PIC-C,PSPsPiPs PİPµCҗC-PsPrCᵣ
CГPİPsCГC,PµCҗC-PİP°P»PëCГCҘ C,P°PеC- C...P°CҗP°PеC,PµCҗPë PеCҗPsPIPсC,PµC± (n=149;
100 %): P°PjPµPSPsCҗPµCҘ (28,2 %), PSpµC±P°CГC,C- PеCҗPsPIPсC,PµC±C- (24,2 %),
C±P°CГC,C- PеCҗPsPIPсC,PµC±C- (2,7 %), PSpµCҗPµPİCᵣP»CҘCҗPSC- PеCҗPsPIPсC,PµC±C-
(21,5 %), C,CҗPëPIP°P»C- PеCҗPsPIPсC,PµC±C- (4,0 %), PSPsCҗPjP°P»CHPSP°
PjPµPSCГC,CҗCᵣP°P»CHPSP° PеCҗPsPIPсC,PµC±P°, C,PsP±C,Ps CҘPеP° PSpµ
PSP°P»PµP¶PëC,CH PrPs P¶PsPrPSPсC— P· PİPsPİPµCҗPµPrPSC-C... PеP°C,PµPİPsCҗC-PN₆ (22,8
%). PµCҗPs P·PjC-PSPë C...P°CҗP°PеC,PµCҗCᵣ PjPµPSCГC,CҗCᵣP°P»CHPSPëC...

PeC₇PsPIP_sC, P_μC_± P»PëC€P_μ C-PSPsPrC- PiPsPIC-PrPsPjP»C_μP»Pë C_μPe PiPsP±C-C_±PSC-
C₇P_μP°PeC_±C-C— C₇ PiP°C_±C-C”PSC, PsPe (PrPëPI. C, P°P±P»PëC_±C₇ PiPsP±C-C_±PSPëC...
C₇P_μP°PeC_±C-PNë).

PJ C, P°P±P»PëC_±C- 1 P·P°P·PSP°C_±P_μPSC- PiPsP±C-C_±PSC- C₇P_μP°PeC_±C-C—
B PIC-PrPiPsPIC-PrPSPs PrPs PeP»P°C₇PëC,,C-PeP°C_±C-C— MedDRA (MedDRA SOCs), PiC₇Ps
C_μPeC- PiPsPIC-PrPsPjP»C_μP»PsC₇C_μ PiC-Pr C_±P°C₇ P·P°C₇C, PsC₇C₇PIP°PSPSC_μ
PiC₇P_μPiP°C₇P°C, PsPj C, P° C—C...PSC_μ C_±P°C₇C, PsC, P°. PJ PjP_μP_μP°C... PePsP_μPSPSC—
PiC₇C₇PiPë PiPsP±C-C_±PSC- P_μC,,P_μPeC, Pë P·P°P·PSP°C_±P_μPSC- C₇ PiPsC₇C_μPrPeC₇
P·PjP_μPSC€P_μPSPSC_μ C_±P°C₇C, PsC, Pë: C_±P°C₇C, C- (≥ 1/100 < 1/10) C- PSP_μC_±P°C₇C, C- (≥
1/1000 < 1/100).

P₇S°C₇C, PsC, P° PIPëP·PSP°C_±P_μPSP° PSP° PiC-PrC₇C, P°PIC- PsP±B₇™ C”PrPSP°PSPëC...
PrP°PSPëC... C_±PsC, PëC₇CH₇PsC... PeP»C-PSC-C_±PSPëC... PrPsC₇P»C-PrP_μP_μPSCH₇ P·P°
C₇C_±P°C₇C, C₇ 332 PiP°C_±C-C”PSC, PsPe (100 %).

P₇Y°P±P»PëC_±C_μ 1

P_μPsP±C-C_±PSC- C₇P_μP°PeC_±C-C—, C,,P°P·P° P_±P_±P_± PeP»C-PSC-C_±PSPëC...
PrPsC₇P»C-PrP_μP_μPSCH₇, N= 332

P ₇ Y°PëC ₇ C, P _μ PjPë PsC ₇ PiP°PSC-PI (MedDRA)	P ₇ S°C ₇ C, C-	P ₇ K _μ C _± P°C ₇ C, C-
P— P±PsPeC ₇ C ₇ PëC ₇ C, P _μ PjPë PeC ₇ PsPIC- C, P° P»C-PjC,,P°C, PëC _± PSPsC— C ₇ PëC ₇ C, P _μ PjPë		P°PSP _μ PjC-C _μ
P ₇ h _μ C, P°P±PsP»C-P·Pj C, P° PiPsC ₇ C ₇ C€P _μ PSPSC _μ PsP±PjC-PSC ₇ C ₇ P _μ C _± PsPiPëPS	PiC-PrPiPëC%P _μ PSPSC _μ PjP°C ₇ Pë C, C-P»P°	P·PSPëP _μ P _μ PSPSC _μ PjP°C ₇ Pë C, C-P»P°, PiC-PrPiPëC%P _μ PSPëPNë P°PiP _μ C, PëC,
P _μ C ₇ PëC...C-C _± PSC- C ₇ PsP·P»P°PrPë	PiC ₇ PëPiPSC-C _± P _μ PSPëPNë PSP°C ₇ C, C ₇ C-PNë, PiPsC ₇ C ₇ C€P _μ PSPSC _μ C ₇ PSC ₇ , PSP _μ C ₇ PIPsP·PSC-C ₇ C, CH, P·PSPëP _μ P _μ PSPSC _μ P»C-P±C-PrPs, P·PjC-PSPë PSP°C ₇ C, C ₇ PsC ₇	P·P°PSP _μ PiPsPePsC”PSPSC _μ , PrP _μ PiC ₇ P _μ C ₇ C-C _μ , P»P°P±C-P»CH ₇ PS-C ₇ C, CH PSP°C ₇ C, C ₇ PsC ₇
P— P±PsPeC ₇ PSP _μ C ₇ PIPsPIP _s C— C ₇ PëC ₇ C, P _μ PjPë	PiPsP»PsPIPSPëPNë P±C-P»CH ₇ , PjC-PiC ₇ P _μ PSCH ₇	PiPsC ₇ C ₇ C€P _μ PSPSC _μ PIP _μ PiP _μ C, P°C, PëPIPsPSC— C ₇ P _μ PiC ₇ P»C _μ C _± C-C—, PiPsC ₇ C ₇ C€P _μ PSPSC _μ C ₇ PIP°PiPë
P— P±PsPeC ₇ PsC ₇ PiP°PSC-PI P·PsC ₇ C ₇		C ₇ C ₇ C...C-C ₇ C, CH PsC _± P _μ PNë
P— P±PsPeC ₇ PsC ₇ PiP°PSC-PI C ₇ P»C ₇ C...C ₇ C, P° PIP _μ C ₇ C, PëP±C ₇ P»C _μ C ₇ PSPsPiPs P°PiP°C ₇ P°C, C ₇		PrP·PIC-PS C ₇ PIC ₇ C...P°C...
P— P±PsPeC ₇ C ₇ P _μ C ₇ C _± C _μ		PSP _μ C ₇ PiP _μ C _± PëC,,C-C _± PSC- C _± PëC ₇ PeC ₇ P»C _μ C, PsC ₇ PSC- C ₇ PsP·P»P°PrPë, PiPsC ₇ PëP»P _μ PSP _μ C ₇ P _μ C ₇ C _± P _μ P±PëC, C, C _μ
P— P±PsPeC ₇ C ₇ C ₇ PrPëPS		P°C ₇ C, P _μ C ₇ C-P°P»CH ₇ PSP° PiC-PiPsC, P _μ PSP·C-C _μ
P— P±PsPeC ₇ PrPëC...P°P»CH ₇ PSPsC— C ₇ PëC ₇ C, P _μ PjPë, PsC ₇ PiP°PSC-PI PiC ₇ C ₇ PrPSPsC— PeP»C-C, PePë C, P° C ₇ P _μ C ₇ P _μ PrPsC ₇ C, C-PSPSC _μ		PrPëC ₇ PiPSPsP _μ

P— P±PsPeCf C€P»CfPSPePsPIPs-PeP€C€PePsPIPsPiPs C,CfP°PeC,Cf	PSCfPrPsC,P°, P±C-P»CH Cf P¶P€PIPsC,C-, PjPµC,PµPsCfP€P·Pj, P·PrCfC,C,Cf P¶P€PIPsC,P°, P±P»CfPIP°PSPSCf	PrC-P°CfPµCf, P·P°PiPsCf, PrP€CfPePsPjC,,PsCfC, Cf C±PµCfPµPIPsC-PN€ PiPsCfPsP¶PSP€PSC-, P·P°PiP°P»PµPSPSCf C€P»CfPSPePsPIPs-PeP€C€PePsPIPsPiPs C,CfP°PeC,Cf, PiC-PSPiC-PIC-C,
P— P±PsPeCf C€PeC-CfP€ C,P° PiC-PrC€PeC-CfPSPsC— PeP»C-C,PePsPIP€PSP€	P°PePSPµ, P°P»PsPiPµC†C-Cf	CfCfC...C-CfC,CH C€PeC-CfP€, PiC-PiPµCfPiC-PrCfPsP·, CfPIPµCfP±C-P¶, PiC-CfCfCfC,P€P·Pj, PsPSC-C...PsPeP»P°P·C-Cf, P»CfPiP°, PrPµCfPjP°C,P€C,, PiPsCfCfC€PµPSPSCf CfPsCfC,Cf PIPsP»PsCfCfCf, CfPµP°PeC†C-C— C,,PsC,PsC†CfC,P»P€PIPsCfC,C-, P·PjC-PSP€ PiC-PiPjPµPSC,P°C†C-C—
P— P±PsPeCf PsPiPsCfPSPs- CfCfC...PsPIPsC— CfP€CfC,PµPjP€ C,P° CfPiPsP»CfC±PSPsC— C,PeP°PSP€PSP€	P±C-P»CH Cf CfPiP€PSC-	P±C-P»CH Cf PeC-CfC,PeP°C..., PjBf™ CfP·PsPIC- CfCfPrPsPjP€, P±C-P»CH Cf PeC-PSC†C-PIPeP°C..., PIC-PrC†CfC,C,Cf C,CfP¶PePsCfC,C- Cf PeC-PSC†C-PIPeP°C...
P— P±PsPeCf PSP€CfPsPe C,P° CfPµC±PsPIP€PrC-P»CHPSPsC— CfP€CfC,PµPjP€		C-PSC,,PµPeC†C-Cf CfPµC±PsPIP€PIC-PrPSP€C... C€P»CfC...C-PI
P— P±PsPeCf CfPµPiCfPsPrCfPeC,P€PIPsC— CfP€CfC,PµPjP€ C,P° PjPsP»PsC±PSP€C... P·P°P»PsP·	PrP€CfPePsPjC,,PsCfC, Cf PjPsP»PsC±PSP€C... P·P°P»PsP·P°C..., PeC-CfC,P° CfC»C±PSP€PeC-PI, PiCfP€PiP»P€PIP€, PjP°C,PePsPIC-/ PIP°PiC-PSP°P»CHPSC-PeCfPsPIPsC,PµC†C-, PI C.,C±. PeCfPsPIPsPjP°P·P°PSPSCf	PIP°PiC-PSP°P»CHPSP€PN€ PeP°PSPPrP€PrPsP·, PICfP»CHPIPsPIP°PiC-PSP°P»CHPSP° CfCfC...C-CfC,CH, PIP€PrC-P»PµPSPSCf P·C-CfC,P°C,PµPIP€C... PsCfPiP°PSC-PI, P±C-P»CH Cf PrC-P»CfPSC†C-PjP°P»PsPiPs C,P°P·P°, P°C,CfPsC,,C-C±PSP€PN€ PICfP»CHPIPsPIP°PiC-PSC-C,, P·P±C-P»CHC€PµPSPSCf PjPsP»PsC±PSP€C... P·P°P»PsP·, PeC-CfC,PsP·PSPs-C,,C-P±CfPsP·PSC-P·P°C...PIPsCfCfPIP°PSPSCf PjPsP»PsC±PSP€C... P·P°P»PsP·, PSP°PiCfCfP±P°PSPSCf PjPsP»PsC±PSP€C... P·P°P»PsP·
P— P°PiP°P»CHPSC- CfPsP·P»P°PrP€ C,P° PjC-CfC†PµPIC- CfPµP°PeC†C-C—	P°CfC,PµPSC-C±PSC-CfC,P°PSP€, PrCfP°C,C-PIP»P€PIC-CfC,CH	PSP°P±CfCfPe

P—PSP€P¶PµPSPSCf PjC-PSPµCfP°P»CHPSPsC— C%oC-P»CHPSPsCfC,C- PeC-CfC,PePsPIPsC— C,PeP°PSP€PSP€

Pj PiCfPsC†PµCfC- PSPµPePsPSC,CfPsP»CHPSPsPIP°PSPsPiPs PeP»C-PSC-C±PSPsPiPs PrPsCfP»C-PrP¶PµPSPSCf P·P° CfC±P°CfC,CH 111 PiP°C†C-C”PSC,PsPe PiC-PrP»C-C,PePsPIPsPiPs PIC-PeCf (PIC-PePsPj PIC-Pr 12 PrPs <18 CfPsPeC-PI), CfPeC-PsC,CfP€PjCfPIP°P»P€ C,PµCfP°PiC-Cf PrC-C”PSPsPiPµCfC,PsPj, C,P°P±P»PµC,PeP°PjP€ 2 PjPi, 103 PiP°C†C-C”PSC,PeP°Pj PIP€PjC-CfCfPIP°P»P€ P¶P©P¶P¶. PµCfP€P±P»P€P·PSPs Cf 72 % CfC±P°CfPSP€PeC-PI PrPsCfP»C-PrP¶PµPSPSCf CfPiPsCfC,PµCfC-PiP°P»PsCfCf P·PSP€P¶PµPSPSCf P¶P©P¶P¶ PiPsPiPµCfPµPePsPIPsPiPs PIC-PrPrC-P»Cf C...CfPµP±C,P° (L2 Bf” L4) PiC-CfP»Cf 12 PjC-CfCfC†C-PI P·P°CfC,PsCfCfPIP°PSPSCf PiCfPµPiP°CfP°C,Cf (PrP€PI. CfPsP·PrC-P» B«PhCfPsP±P»P€PIPsCfC,C- P·P°CfC,PsCfCfPIP°PSPSCfB»).

PµPsPIC-PrPsPjP»PµPSPSCf PiCfPs PiC-PrPsP·CfCfPIP°PSC- PiPsP±C-C±PSC- CfPµP°PeC†C-C—

P_μPsPIC-PrPsPjP»P_μPSPSC_Ц P_иС_ТPs P_иC-PrPsP·С_ТС_ТPIP°PSC- P_иPsP±C-C±PSC-
С_ТP_μP°PeC†C-C— C_р P_иP_μС_ТC-PsPr P_иPsC_ГC,PjP°С_ТPeP_μC,PëPSPiPsPIPsPiPs
C_ГP_иPsC_ГC,P_μС_ТP_μP_ГP_μPSPSC_Ц C” PrC_рP_ГP_μ PIP°P_ГP»PëPIPëPjPë. P_иP_μ PrP°C”
PjPsP_ГP»PëPIC-C_ГC,С_Т P·PrC-PN₂C_ГPSC_ТPIP°C,Pë PePsPSC,С_ТPsP»С_Т
C_ГP_иC-PIPIC-PrPSPsC€P_μPSPSC_Ц PePsС_ТPëC_ГC,С_Т/С_ТPëP·PëPe P·P°C_ГC,P_сC_ГC_рPIP°PSPSC_Ц
P»C-PeP°С_ТC_ГС_ТPePëC... P·P°C_ГP_сP±C-PI. P_ТP_μPrPëC±PSC- P_иС_ТP°C†C-PIPSPëPePë
P_иPsPIPëPSPSC- P_иPsPIC-PrPsPjP»C_ЦC,Pë P_иС_ТPs P_иC-PrPsP·С_ТС_ТPIP°PSC- P_иPsP±C-C±PSC-
С_ТP_μP°PeC†C-C—.

P_ГP_μС_ТPjC-PS P_иС_ТPëPrP°C,PSPsC_ГC,-. 5 С_ТPsPePë.

PjPjPsPIPë P·P±P_μС_ТC-PiP°PSPSC_Ц. P>C-PeP°С_ТC_ГС_ТPePëPN₂ P·P°C_ГC-P± PSP_μ
P_иPsC,С_ТP_μP±C_рC” C_ГP_иP_μC†C-P°P»С_ТPSPëC... C,P_μPjP_иP_μС_ТP°C,C_рС_ТPSPëC... C_рPjPsPI
P·P±P_μС_ТC-PiP°PSPSC_Ц. P—P±P_μС_ТC-PiP°C,Pë PI PsС_ТPëPiC-PSP°P»С_ТPSC-PN₂
C_рP_иP°PePsPIC†C- PrP»C_Ц P·P°C...PëC_ГC,C_р PIC-Pr PIP_иP»PëPIC_р C_ГPIC-C,P»P°.

P—P±P_μС_ТC-PiP°C,Pë PI PSP_μPrPsC_ГC,C_рP_иPSPsPjC_р PrP»C_Ц PrC-C,P_μPN₂ PjC-C_ГC†C-.

**PjP_иP°PePsPIPeP°. P_μPs 14 C,P°P±P»P_μC,PsPe C_р P±P»C-C_ГC,P_μС_ТC-; P_иPs 2
P°P±Ps 6 P±P»C-C_ГC,P_μС_ТC-PI PI PeP°С_ТC,PsPSPSC-PN₂ PePsС_ТPsP±C†C-.**

P_ТP°C,P_μPiPsС_ТC-C_Ц PIC-PrP_иC_рC_ГPeC_р. P—P° С_ТP_μC†P_μP_иC,PsPj.

P’PëС_ТPsP±PSPëPe. P’P_ТP_Г B«P“P_μPrP_μPsPS P C-C...C,P_μС_ТB», PjPiPsС_ТC%PëPSP°.

**P_ТC-C_ГC†P_μP·PSP°C...PsPrP_ГP_μPSPSC_Ц PIPëС_ТPsP±PSPëPeP° C,P° P°PrС_ТP_μC_ГP°
PjC-C_ГC†C_Ц P_иС_ТPsPIP°PrP_ГP_μPSPSC_Ц PN₂PsPiPs PrC-C_ЦP»С_ТPSPsC_ГC,-.**

P_К-1103, P’C_рPrP°P_иP_μC€C,, PIC_рP». P”P_μPjС_ТP_μC—, 19-21, PjPiPsС_ТC%PëPSP°.