

D. 考察

HIV 耐性検査は治療導入前の施行がガイドライン上勧められており、検査結果によって使用薬剤が変更されることもある。治療の変更等が必要となりうる耐性変異として、RT 領域に K103N と M184V の変異を認めた。いずれの変異も過去にも報告されたものである。K103N の頻度は決して高いものではないが、EFV の投与の際には注意が必要となる変異である。M184V は B 型肝炎に対して核酸アナログ製剤が長期に使用されていた症例であった。過去の

報告書においても言及したが、B 型肝炎の診断を行った場合は、必ず HIV 検査が必要であることを示唆する症例である。一方、PR 領域には 2 例の耐性症例を認め、いずれも L10I・D30N・L33F・N88D を有しており NFV に対する高度耐性が推測された。平成 22 年度の報告書においては、この 2 例は系統樹解析においても近い距離に位置していた。このような薬剤耐性ウイルスの伝搬が危惧され、薬剤耐性検査による疫学調査は今後も必要と考えられた。

RAL は血中 HIV-RNA 量を低下させるスピードが

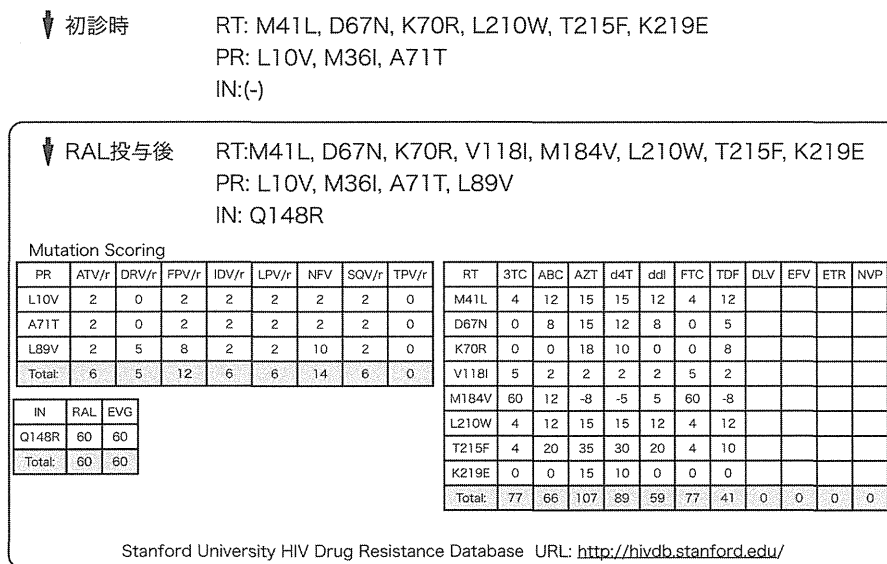


図 6 症例 1 の耐性検査

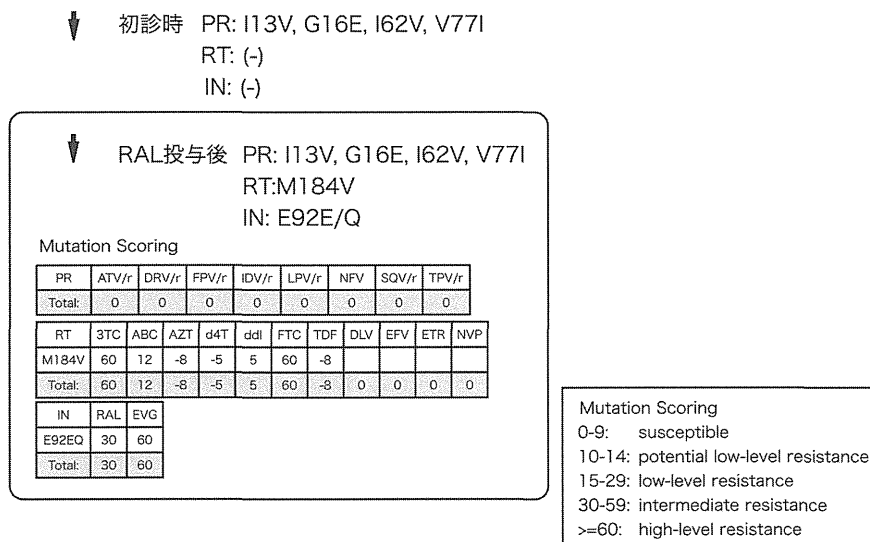


図 7 症例 2 の耐性検査

早いことに加え、副作用や薬物相互作用で問題となることが少ないことが特徴としてあげられる。しかし、耐性獲得に対する genetic barrier が低いことも問題視されている。初回治療を導入後、RT 領域の M184V/I は最初に出現する耐性変異としてよく経験する。今回図で示した 6 症例のうち、症例 1 と症

例 3 は過去に耐性変異を有していたが、残りの 4 症例は RAL 耐性が最初に出現した変異であった。3 症例は M184V も同時に出現していることから、RAL 耐性変異 (N155 と Q148) は M184V/I と同様に早期に耐性獲得に至ることが考えられた。

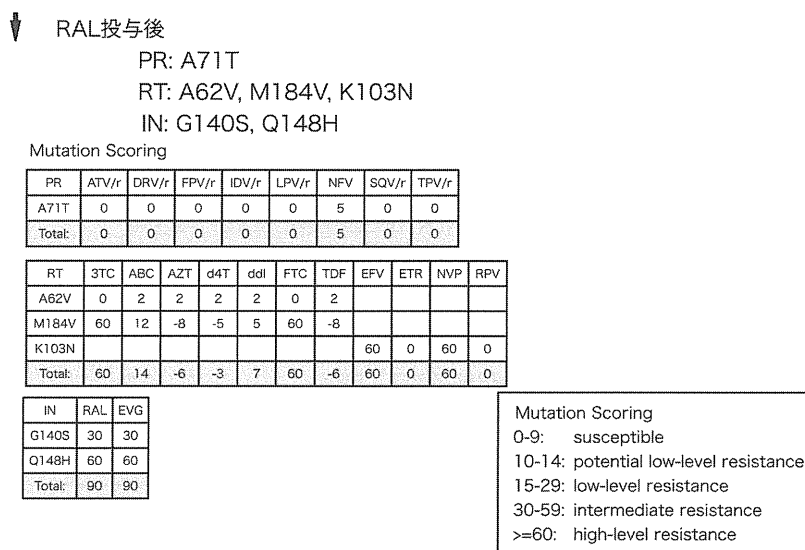


図 8 症例 3 の耐性検査

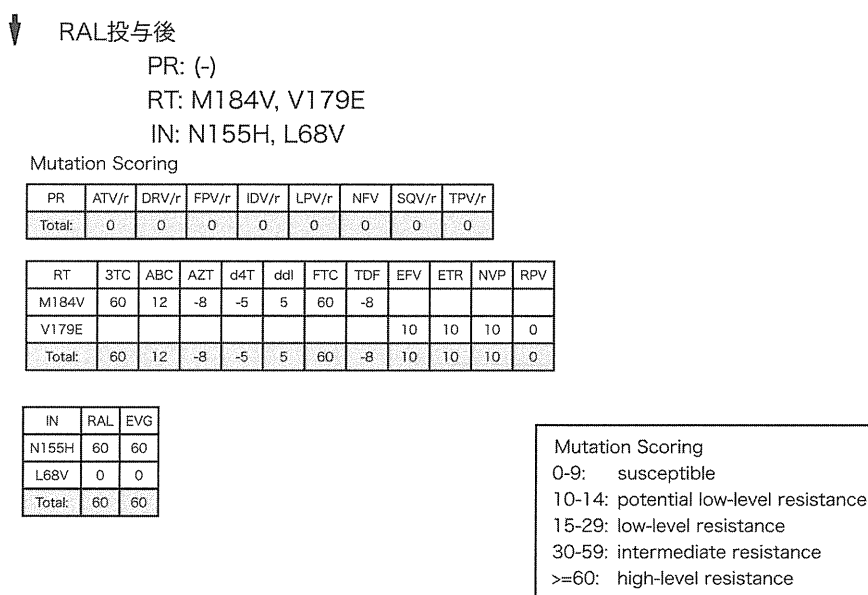


図 9 症例 4 の耐性検査

E. 結論

277 症例がサーベイランスの対象となった。WHO の 2009 年のリストに該当する耐性変異は T69D (1 例)、M184V (1 例)、K219Q (1 例)、T215X (5 例)、K103N (1 例)、D30N+N88D (2 例)、M46L (1 例)、I54T (1 例) に認めるのみであった。2010-2012 年に 6 例の RAL 耐性変異を経験した。RAL はウイルス学的効果や忍容性に優れる一方で、

耐性獲得に対する genetic barrier が低く、耐性変異の出現には注意が必要である。

F. 健康危険情報

該当なし

サブタイプ : B  
PR領域 : 未検査  
RT領域 : 未検査  
IN領域 : N155H

Mutation Scoring

IN	RAL	EVG
N155H	60	60
Total:	60	60

【解析方法】

Seqscape Ver 2.6 (Applied Biosystems) と Stanford University HIV drug resistance database (15-June-2012) を用いた。

Mutation Scoring

0-9: susceptible  
10-14: potential low-level resistance  
15-29: low-level resistance  
30-59: intermediate resistance  
>=60: high-level resistance

図 10 症例 5 の耐性検査 1 回目

サブタイプ : B  
PR領域 : A71V  
RT領域 : T69ST  
IN領域 : Q148K >> N155H

Mutation Scoring

PR	ATV/r	DRV/r	FPV/r	IDV/r	LPV/r	NFV	SQV/r	TPV/r
A71V	0	0	0	0	0	5	0	0
Total:	0	0	0	0	0	5	0	0

RT	3TC	ABC	AZT	d4T	ddl	FTC	TDF	EFV	ETR	NVP	RPV
T69NSTY	0	0	0	0	0	0	0				
Total:	0	0	0	0	0	0	0	0	0	0	0

IN	RAL	EVG
Q148K	60	60
Total:	60	60

図 11 症例 5 の耐性検査 2 回目

▼ RAL投与後

PR: L10I  
 RT: M184V  
 IN: G140AT, Q148R

Mutation Scoring

PR	ATV/r	DRV/r	FPV/r	IDV/r	LPV/r	NFV	SQV/r	TPV/r
L10I	0	0	0	0	0	0	0	0
Total:	0	0	0	0	0	0	0	0

RT	3TC	ABC	AZT	d4T	ddl	FTC	TDF	EFV	ETR	NVP	RPV
M184V	60	15	-10	-10	10	60	-10				
Total:	60	15	-10	-10	10	60	-10	0	0	0	0

IN	RAL	EVG
G140AT	30	30
Q148R	60	60
Total:	90	90

Mutation Scoring  
 0-9: susceptible  
 10-14: potential low-level resistance  
 15-29: low-level resistance  
 30-59: intermediate resistance  
 >=60: high-level resistance

図 12 症例 6 の耐性検査

G. 研究発表

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H. 知的財産権の出願・登録状況  
なし





## 研究成果の刊行に関する一覧

## 研究成果の刊行に関する一覧表 (H22~24年度)

## 書籍

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