

Mechanism of emergence of resistance of T97A during Dolutegravir therapy

K Huik, JM George, SS Kuriakose, N Dee, P Stoll, R Dewar, MA Khan, MT
Rehman, Z Grossman, AK Pau, F Maldarelli

- **Integrase Strand Transfer Inhibitors (INSTIs)**

- are potent antiretrovirals
- are used in first line combination antiretroviral therapy
- efficacy can be compromised by several primary drug resistance mutations
- the role of accessory mutations is unclear

- **INSTI T97A**

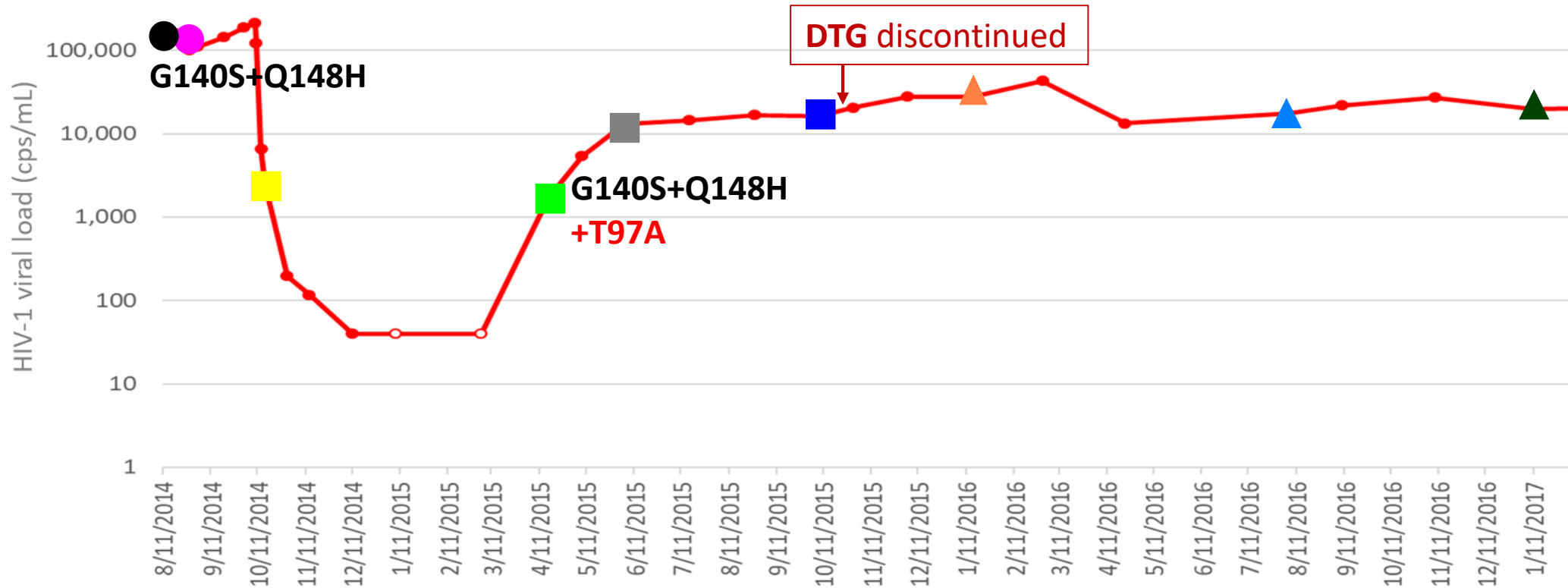
- INSTI accessory mutation
- selected by DTG in treatment experienced patients with pre-existing RAL/EVG resistance mutations
- emerges rapidly after DTG containing therapy
- resulted in a >10 fold increase in phenotypic resistance to DTG (Kuriakose et al. Open Forum Inf Dis 2018)

**Rapid Emergence of T97A During Dolutegravir
Therapy:**

**Does Resistance Emerge as a Single Lineage or as a
Diverse Population?**

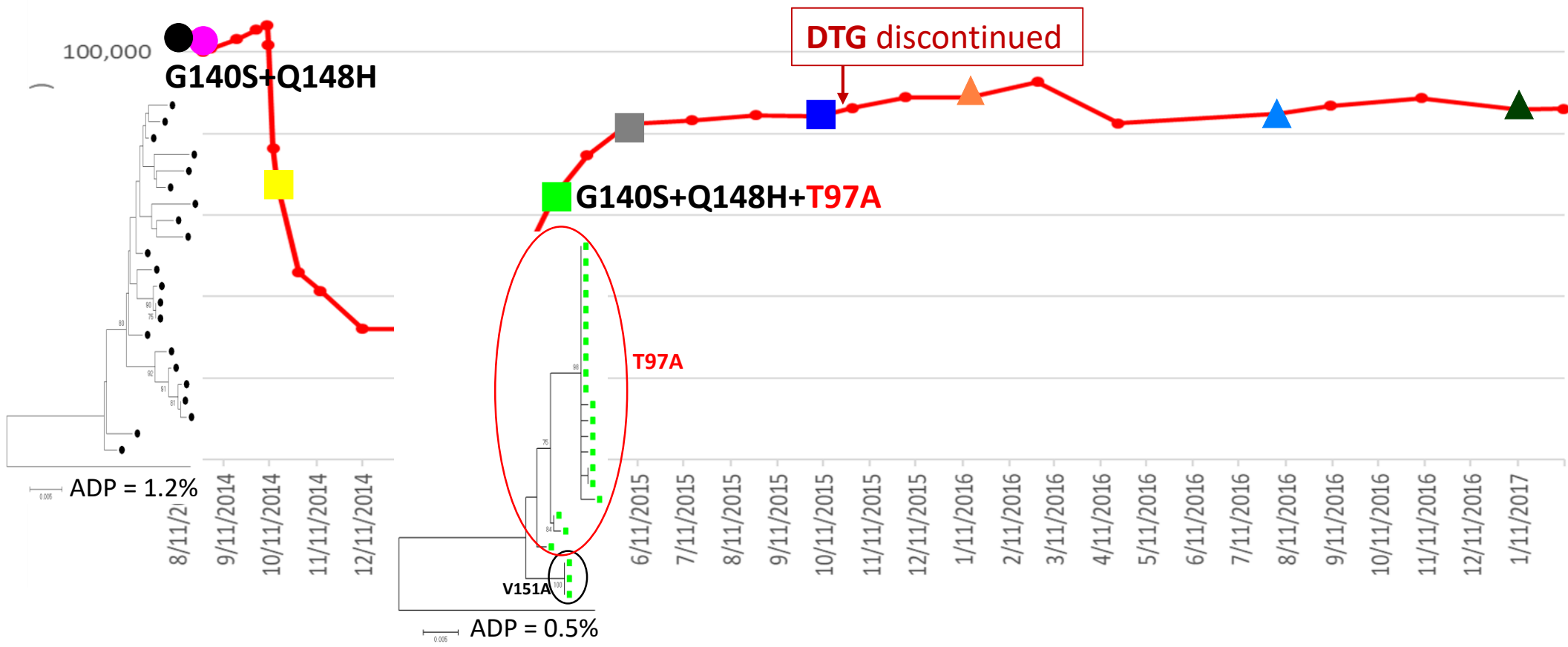
The history of study patient

RAL	ATV+LPV/r+TDF/FTC	DTG + DRV/r + TDF/FTC + MVC	DRV/r + TDF/FTC + MVC	DRV/r + TDF/FTC
-----	-------------------	------------------------------------	-----------------------	-----------------

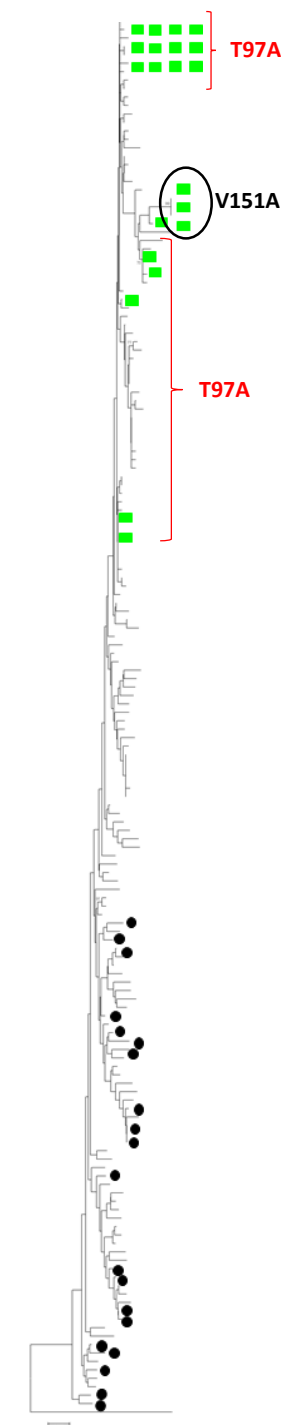


G140S+Q148H							
T97A	0%	85.7%	100%	100%	100%	81.8%	4.8%
V151A		14.3%					

RAL	ATV+LPV/r+TDF/FTC	DTG + DRV/r + TDF/FTC + MVC	DRV/r + TDF/FTC + MVC	DRV/r + TDF/FTC
-----	-------------------	-----------------------------	-----------------------	-----------------



Population 1	Population 2	Population 3
--------------	--------------	--------------



Conclusions

- **T97A:**
 - **Emerges rapidly from a single variant after DTG**
 - **Diminishes slowly after DTG is discontinued**
- **Population shift detected after DTG therapy**

Acknowledgments

Clinical Retrovirology Section, NCI

Frank Maldarelli

Shawn Hill

Camille Lange

Elizabeth Anderson

Monica Gouzoulis

Natalie Lindo

Jennifer Bell

Zehava Grossman

Pamela Harris

National Institute of Allergy and
Infectious Diseases

Alice Pau

The study patient



HIV Dynamics and Replication Program
NCI-Frederick
