

Personalising medical therapy on the rest

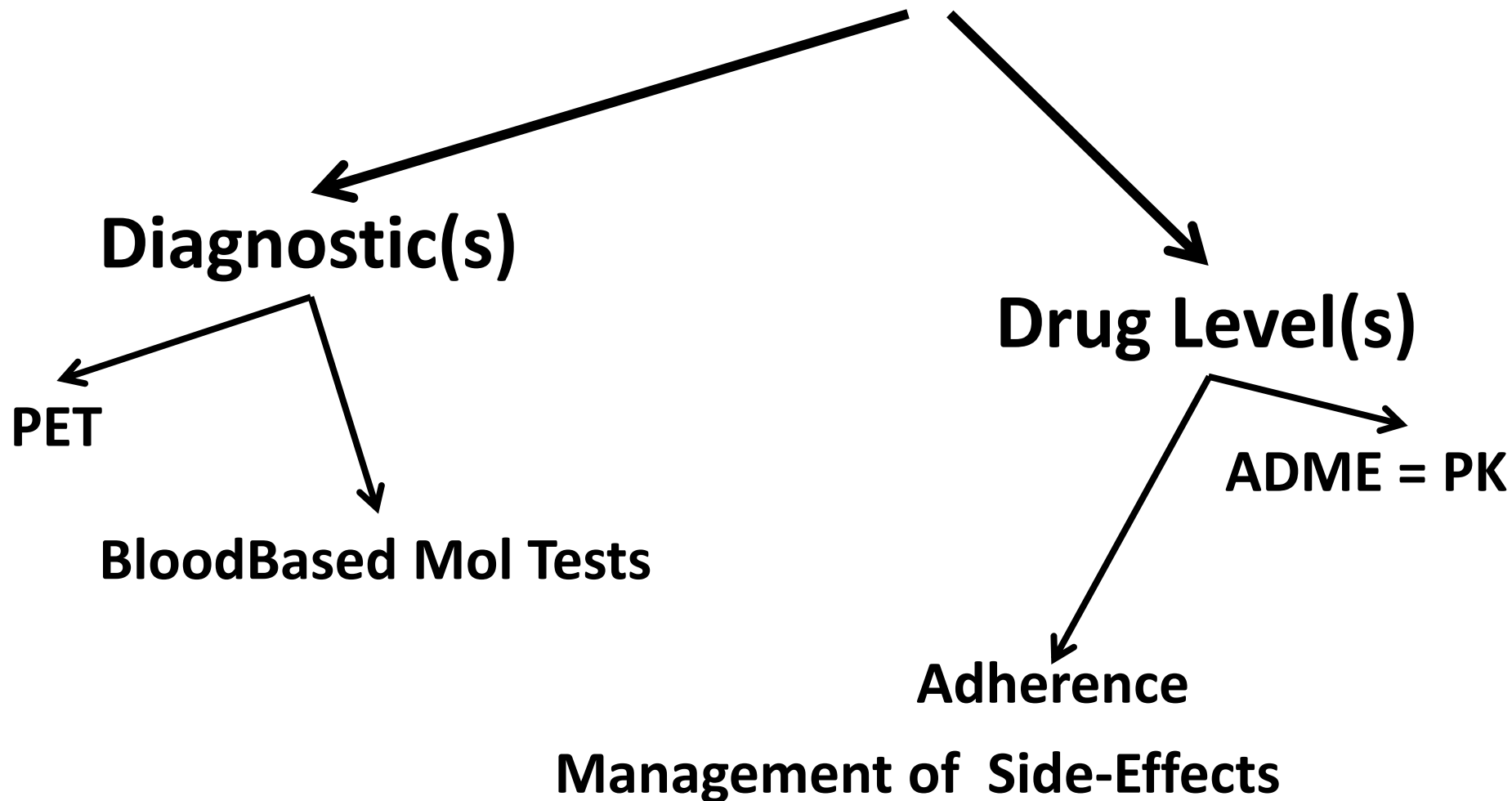
Michael Montemurro



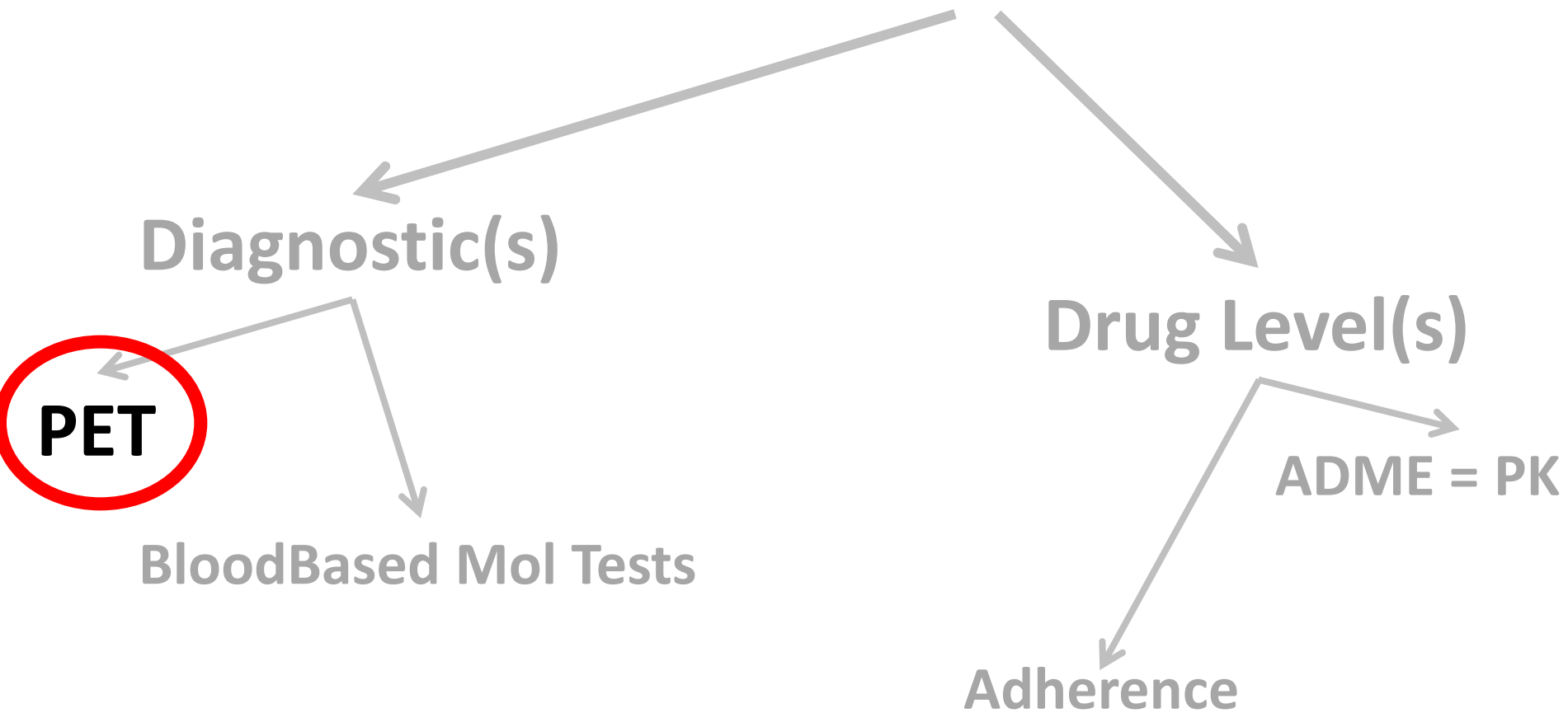
Disclosure slide

- No conflicts of interest

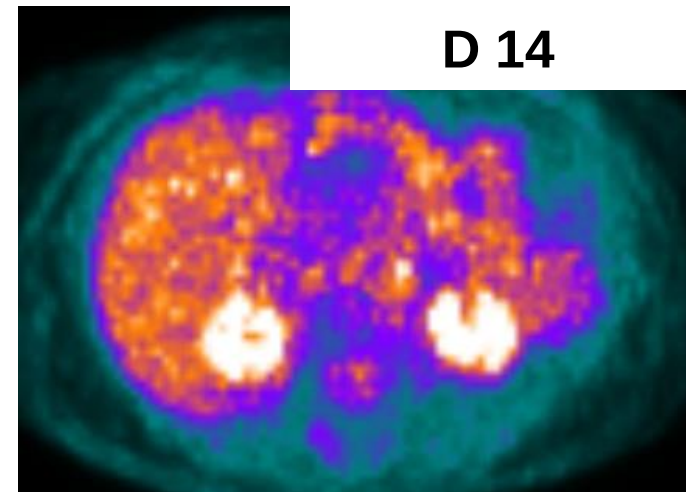
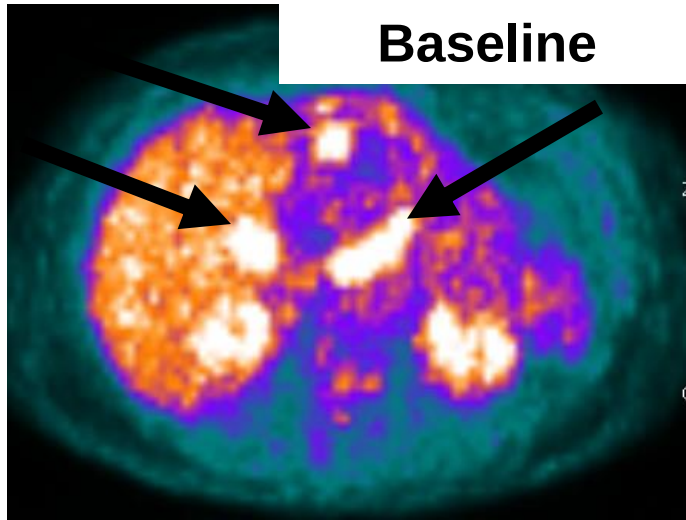
Personalising → Outcome



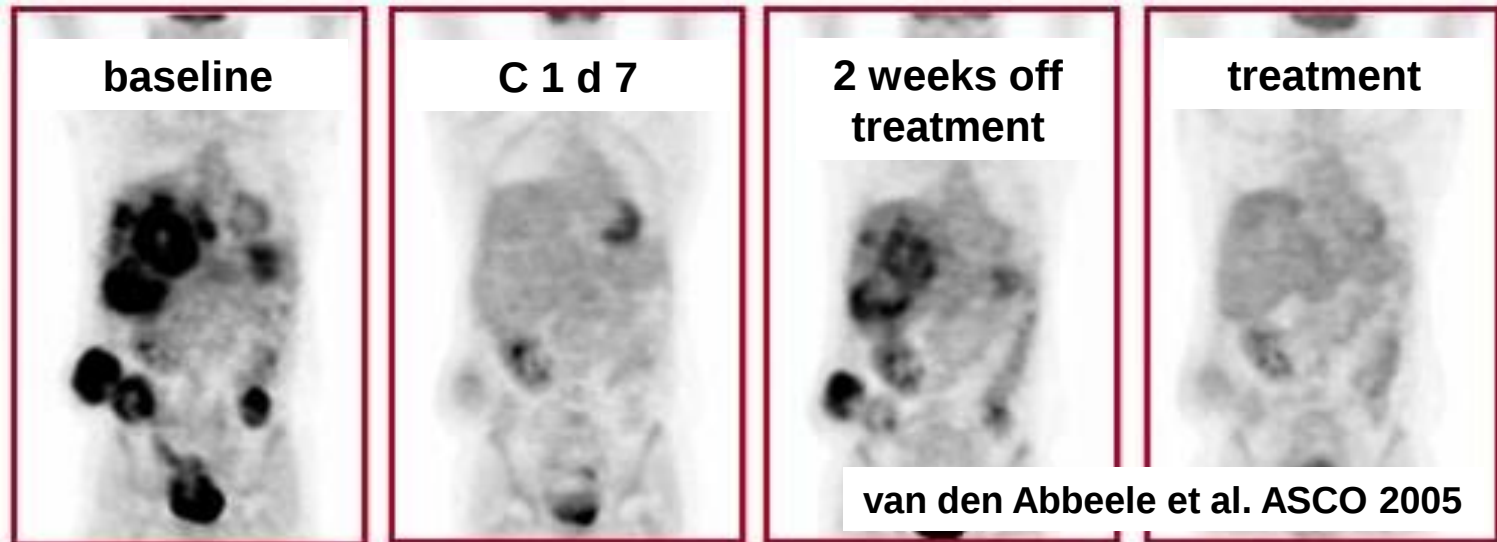
Personalising → Outcome



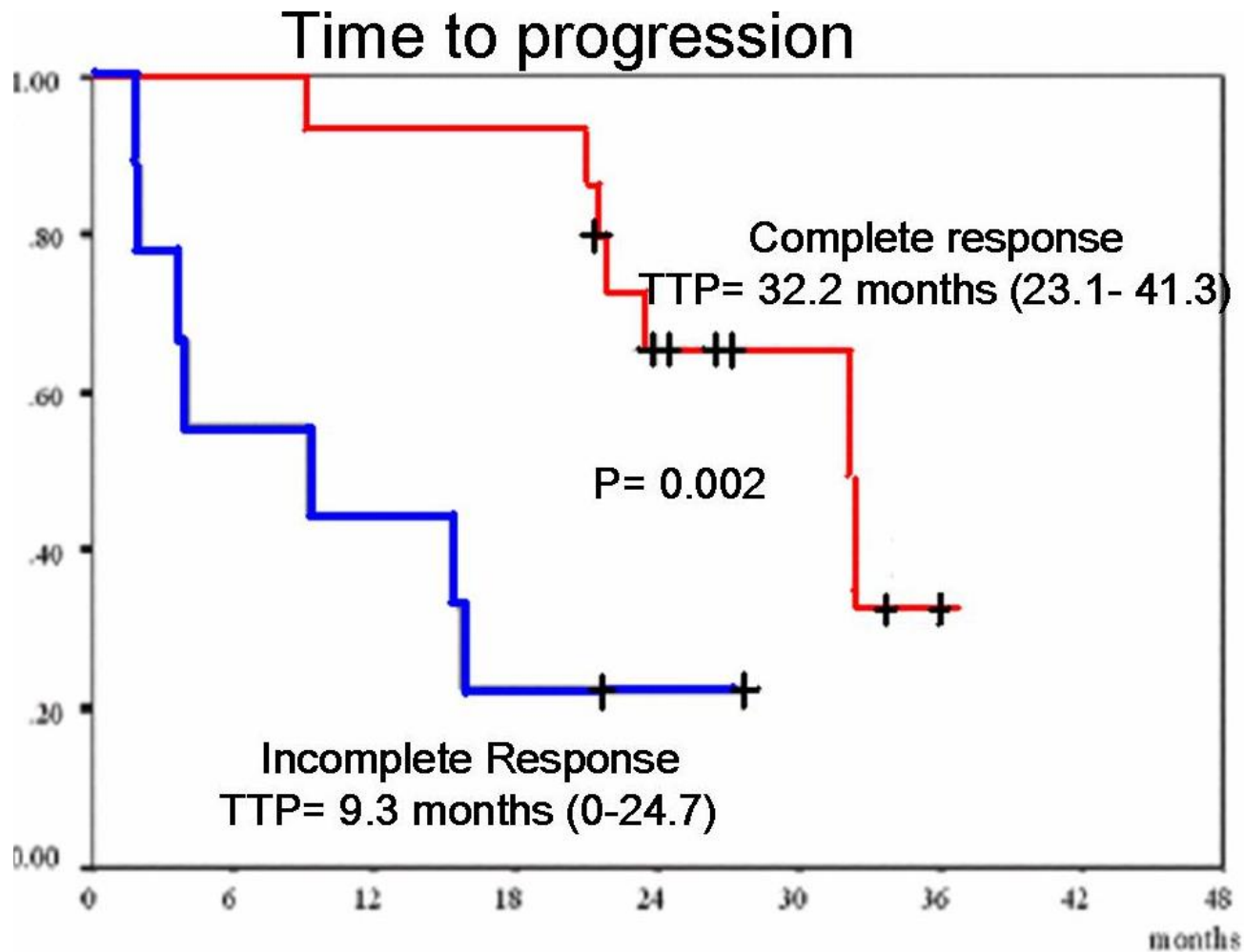
PET – „temporal resolution“



Prior et Montemurro, CHUV Lausanne



PET in 1st-line Imatinib



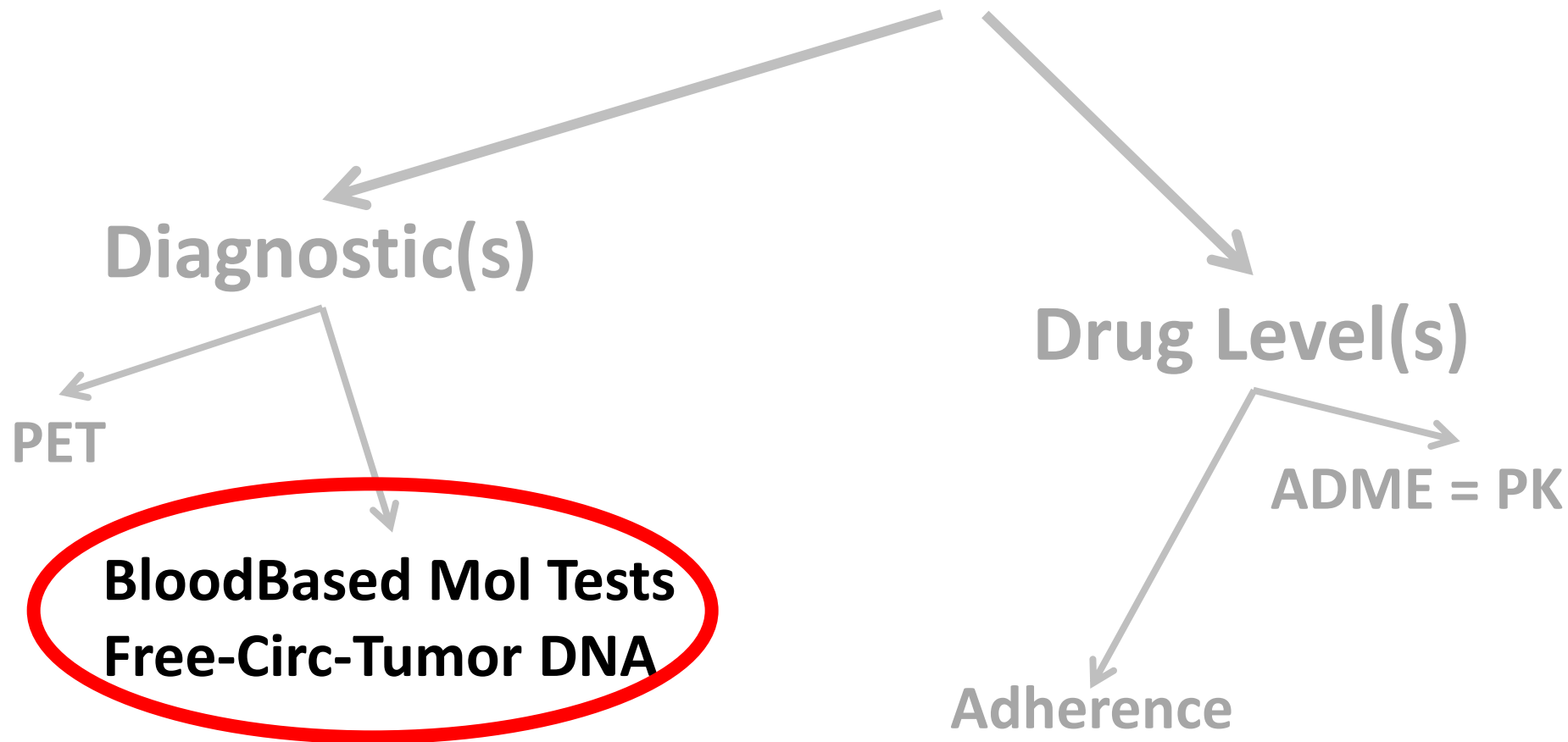
- Early PET response predicts outcome

Role of PET

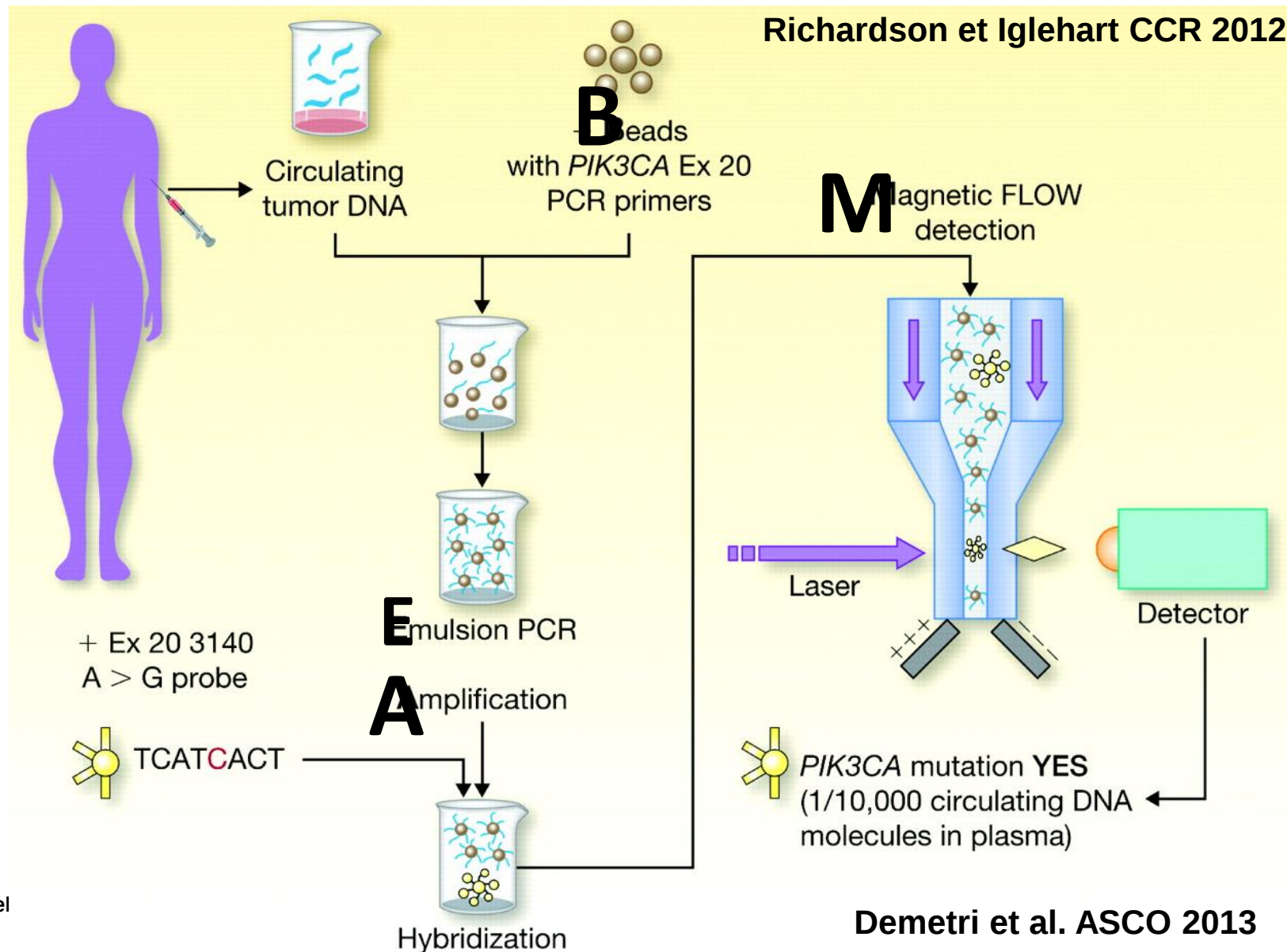
Selected Cases / Situations

- **Early Response Assessment**
 - Neo-adjuvant treatment
 - Selection of treatment for a specific mutation ???
 - CAVE: FDG-neg GIST --- role of baseline PET
- **Increases Detection Rates**
- **Trials**

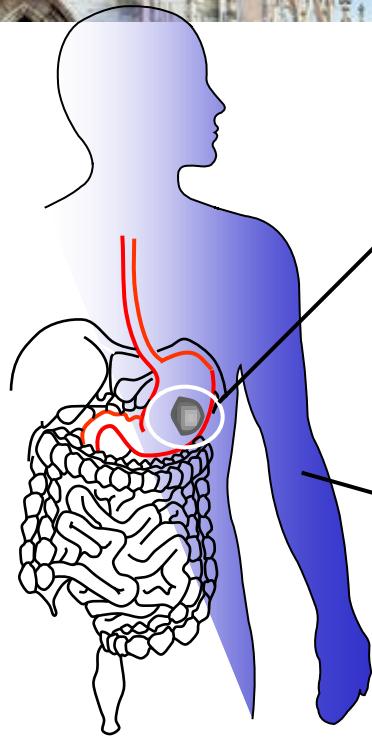
Personalising → Outcome



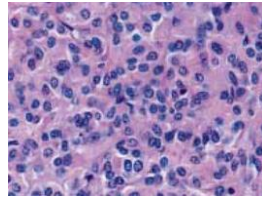
Free Circulating Tumor – fct DNA



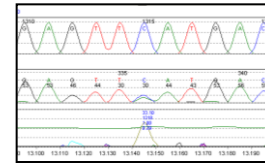
FCT DNA as Biomarker



Tumor Tissue



→ Detection of Mutation(s)



Sanger sequencing

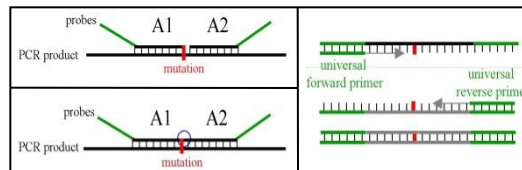
Blood Plasma



→ Free Circulating DNA

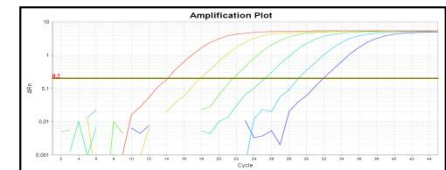


Mutation-Specific Quantification of fcDNA
(known + unknown mutations)



Ligation PCR

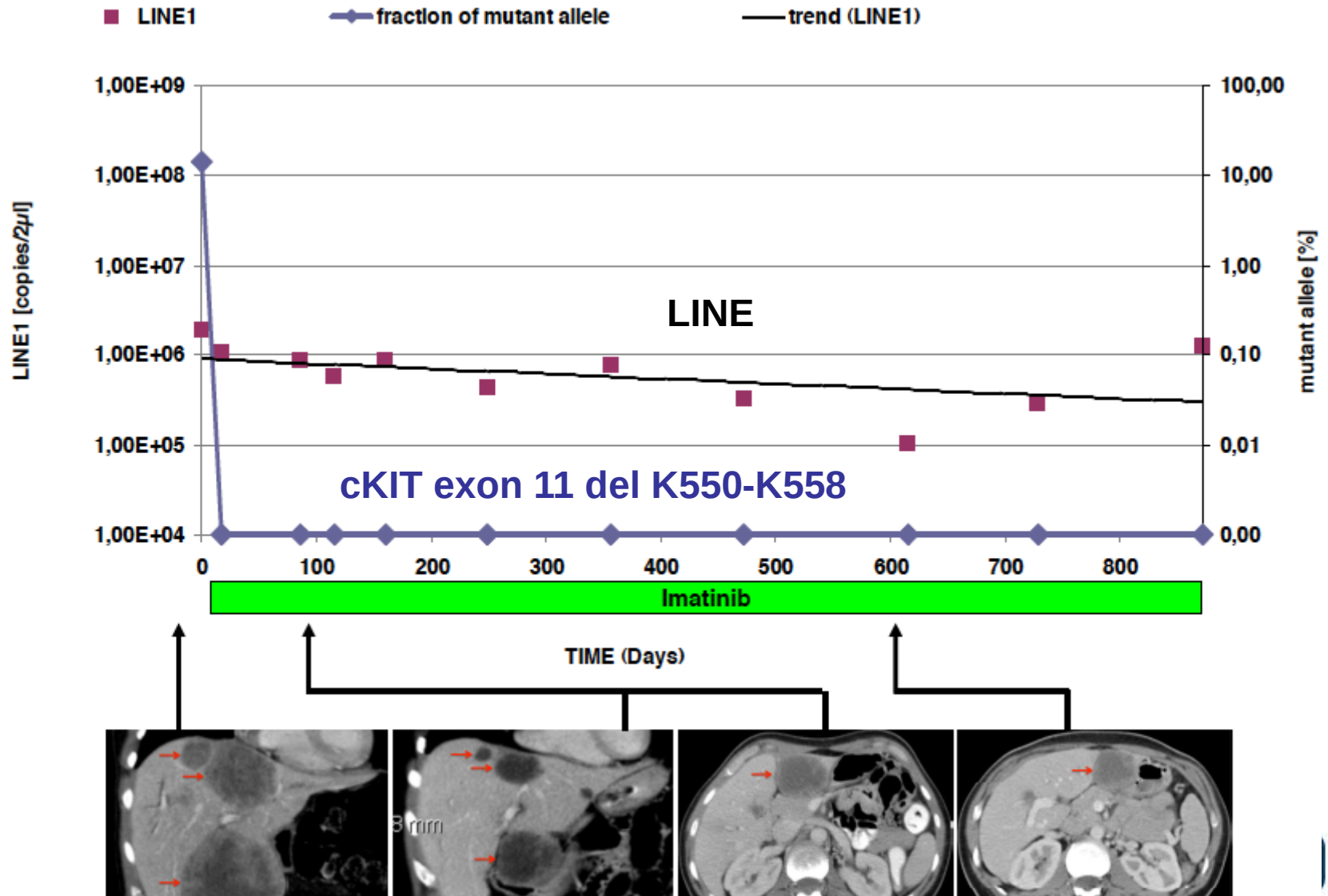
LINE1 Quantification



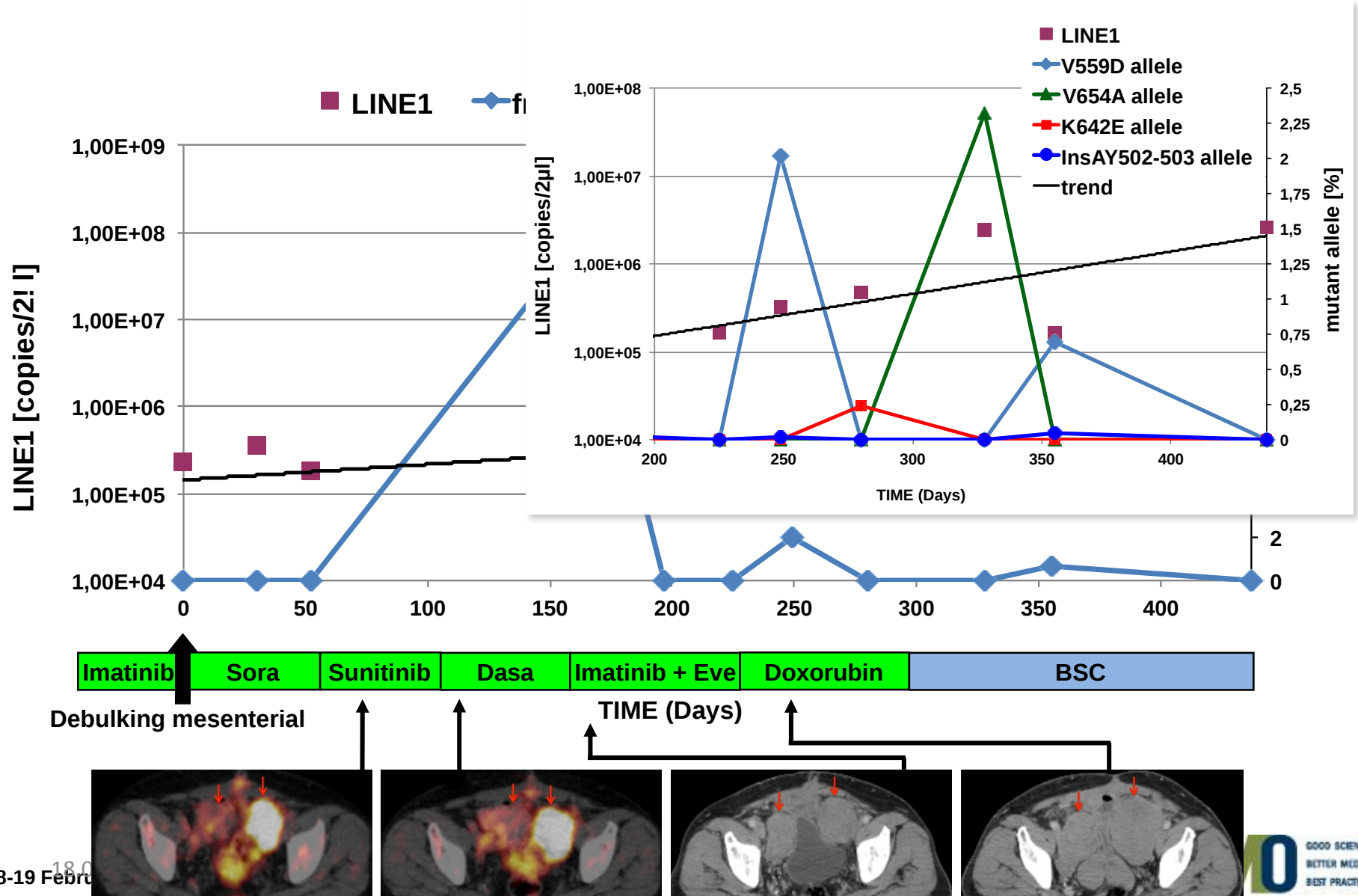
Real Time PCR

Courtesy: Von Bubnoff et al. ASCO 2013

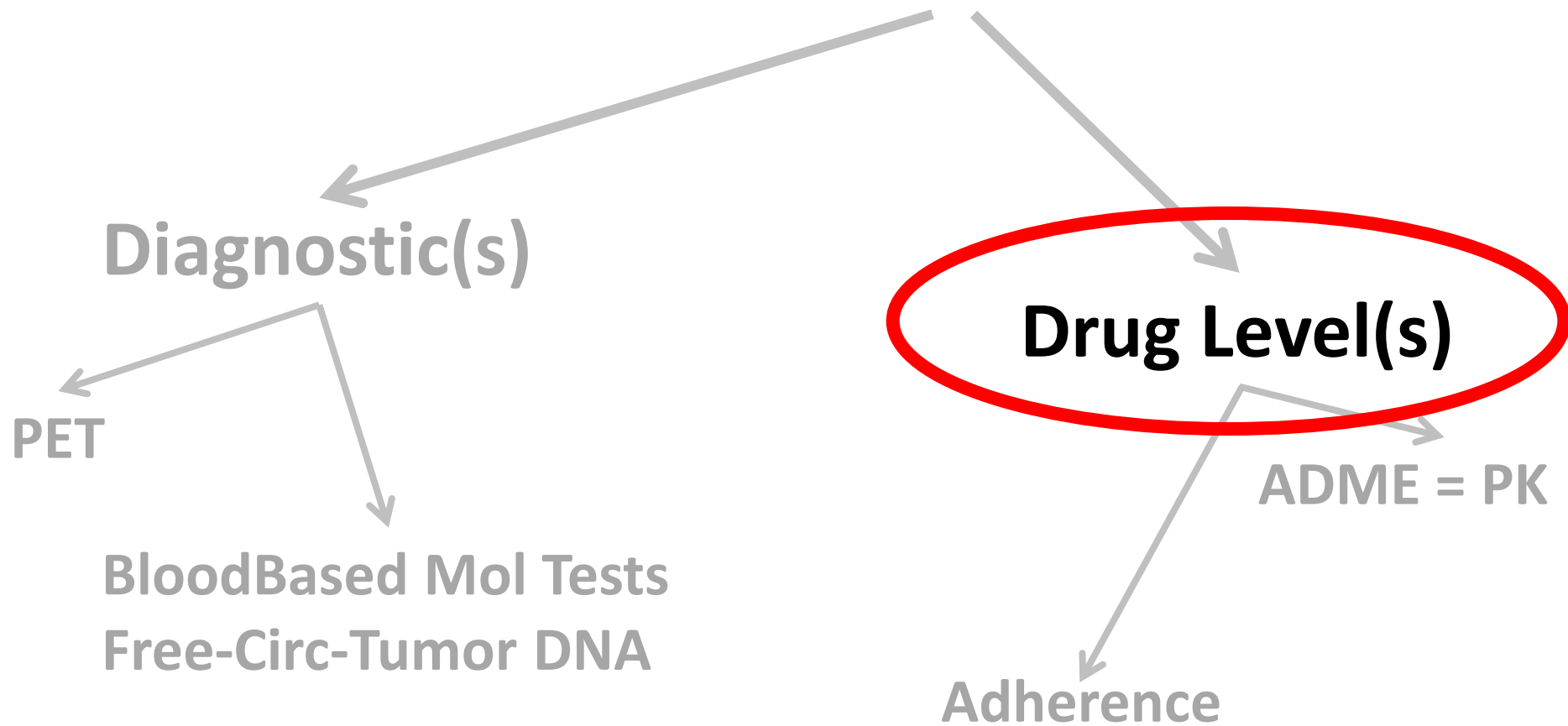
Rapid decrease of mutant fcDNA



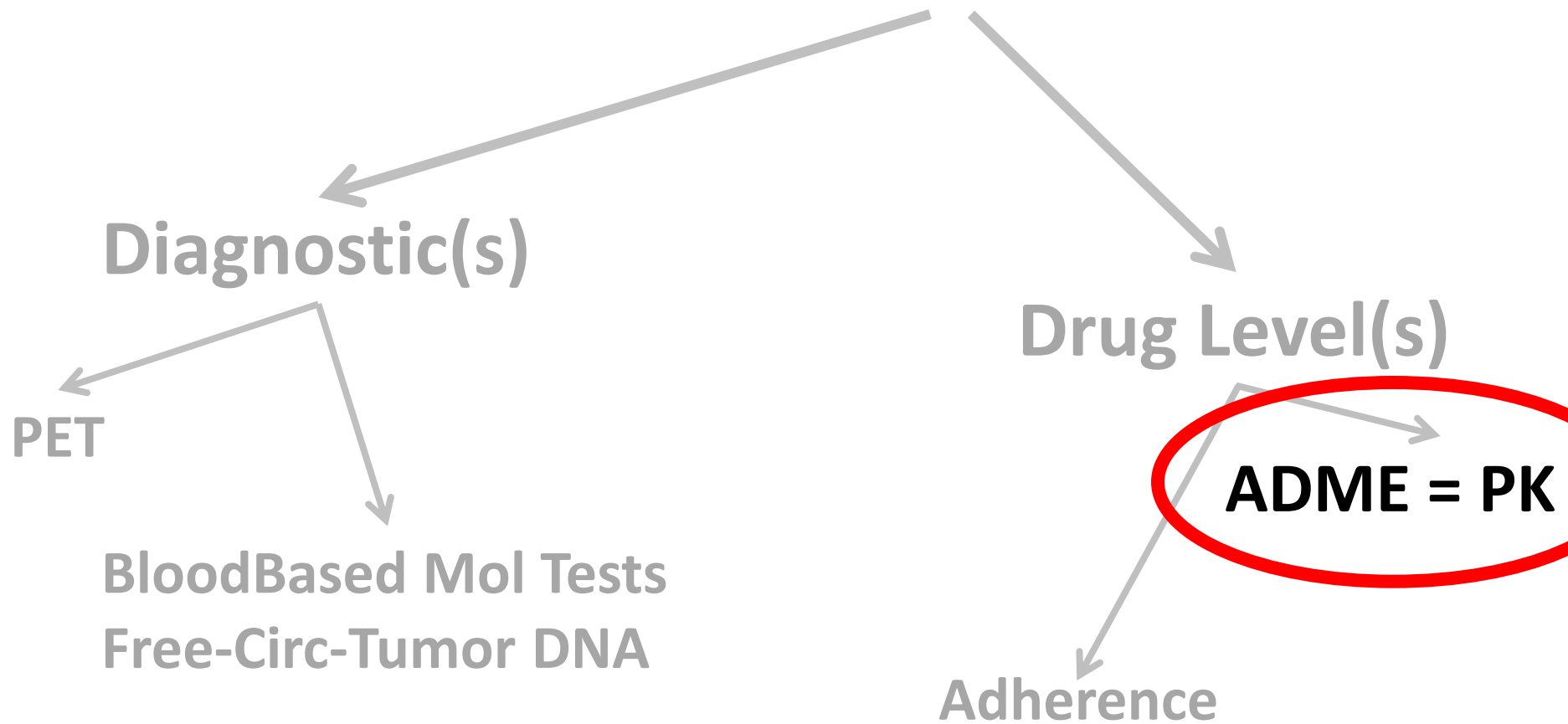
Detection / FU Multiple Clones



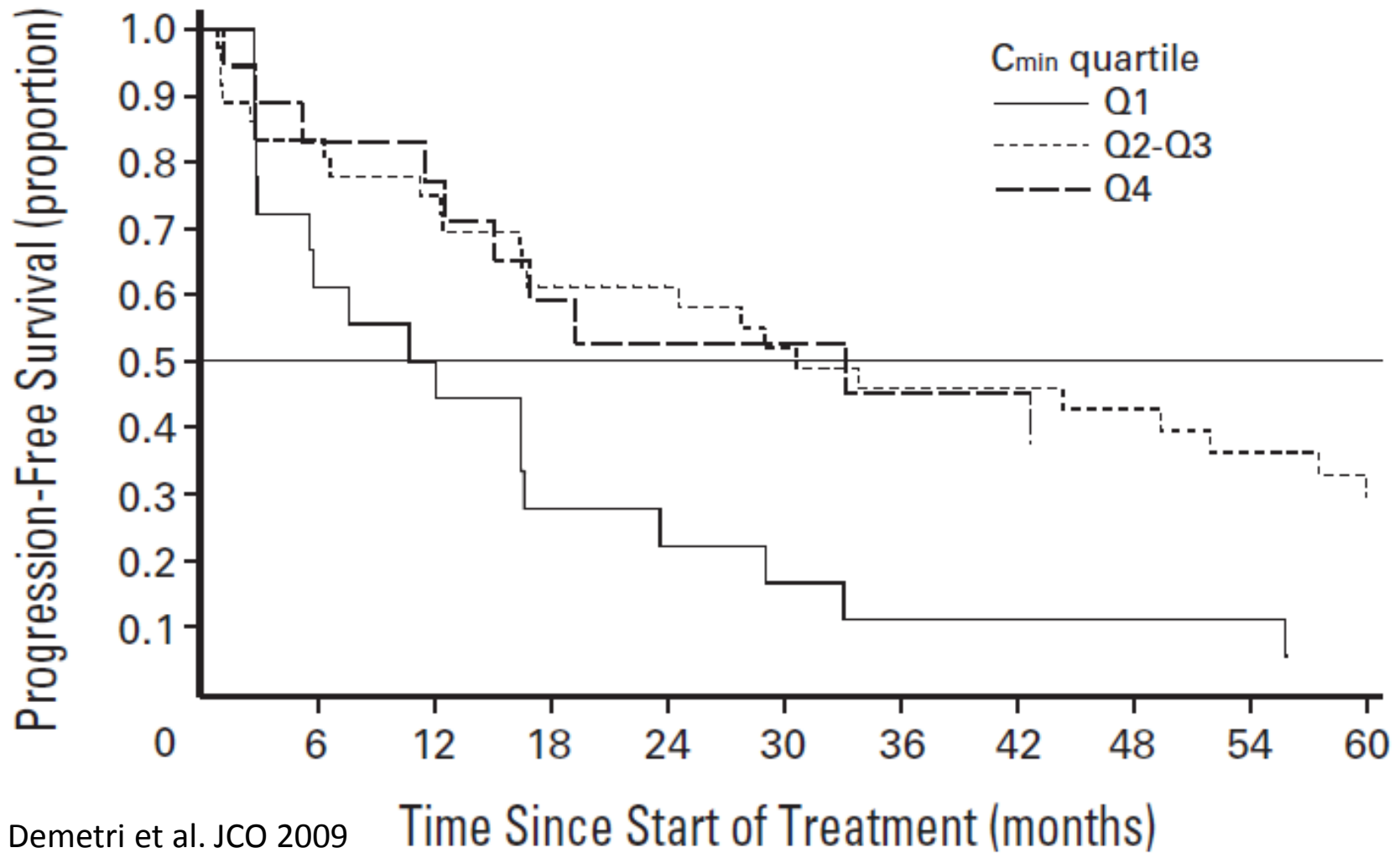
Personalising → Outcome



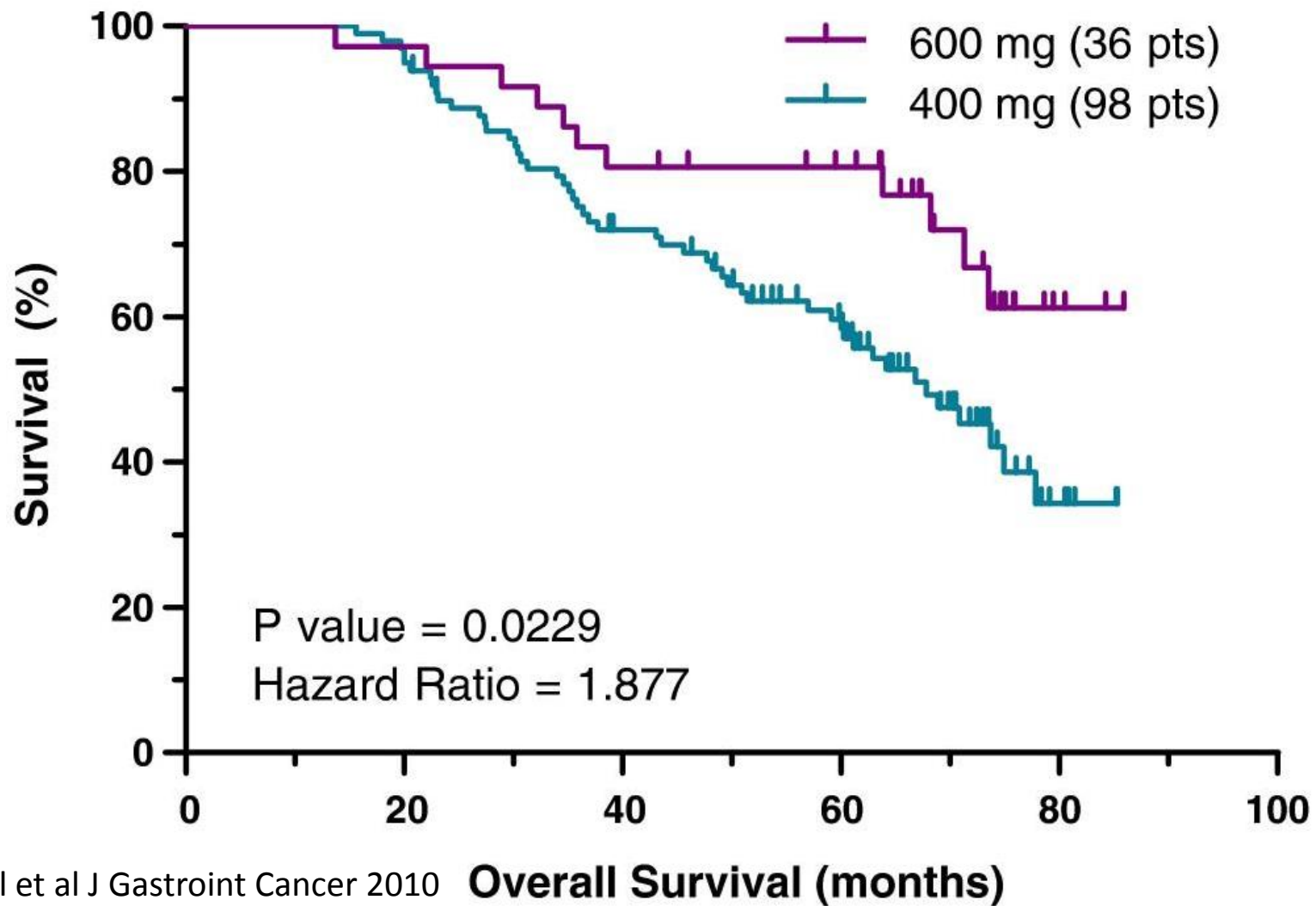
Personalising → Outcome



Imatinib PK - Outcome



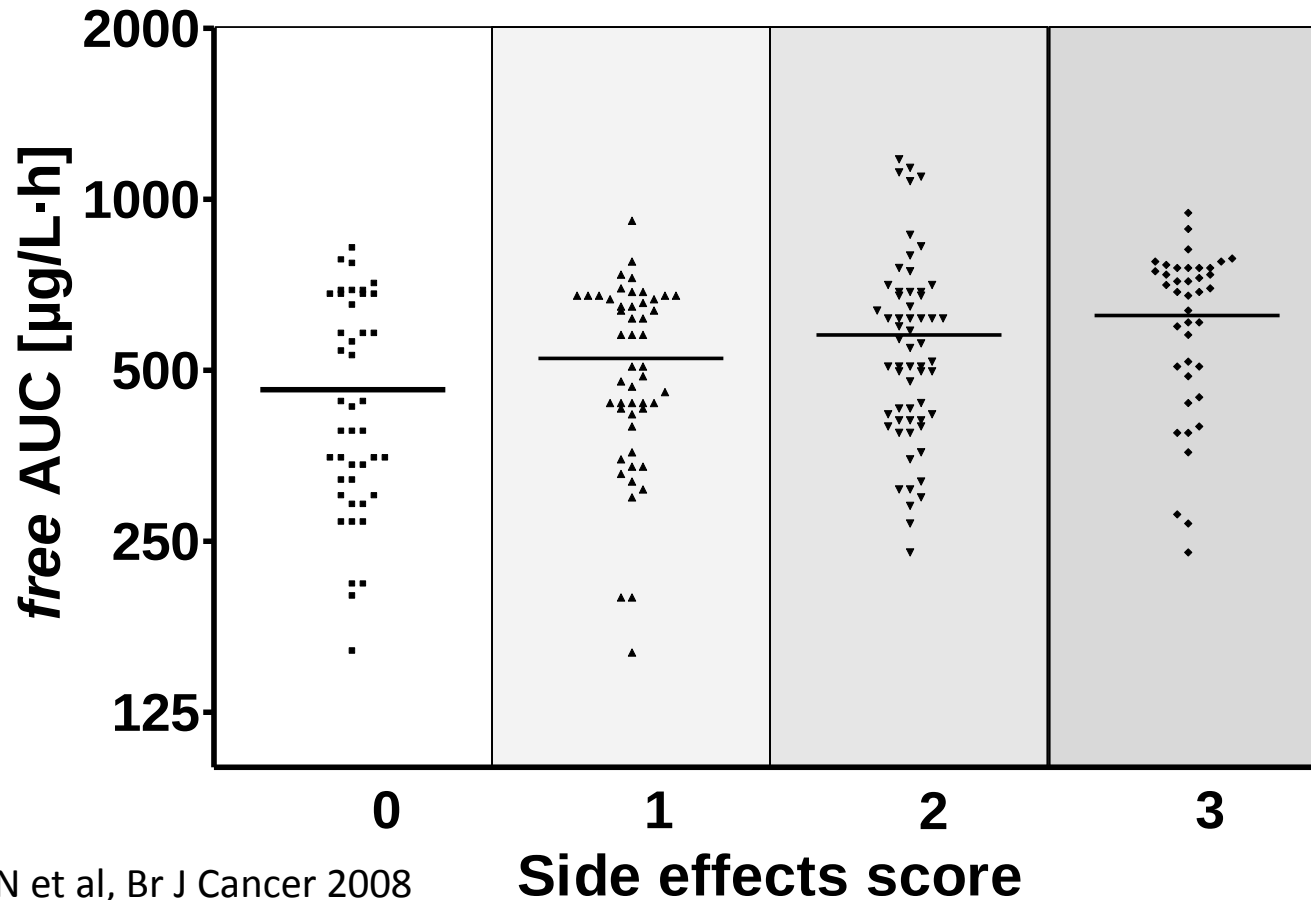
Self Reported Imatinib



Call et al J Gastroint Cancer 2010

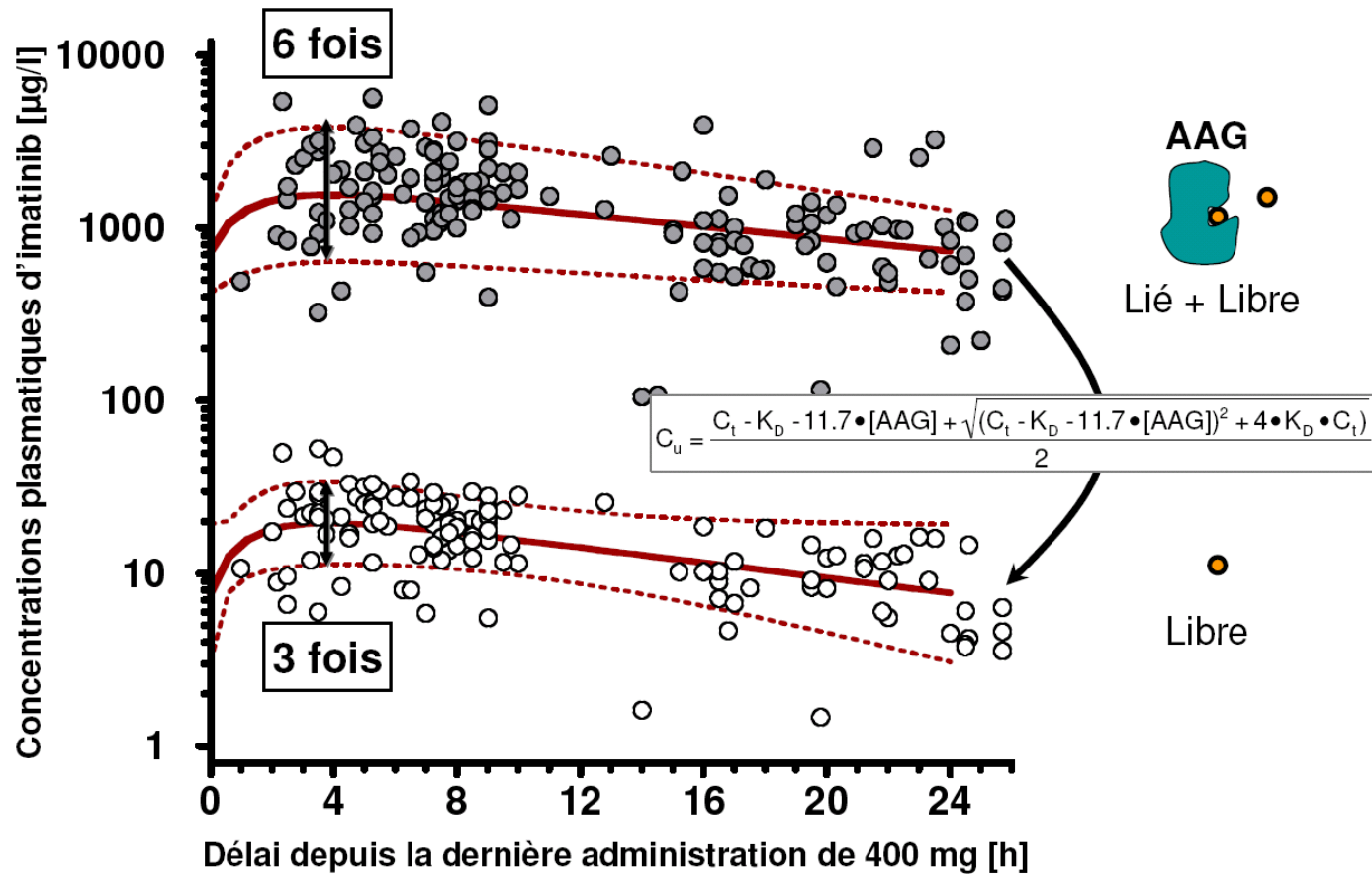
Overall Survival (months)

(free) Drug Level = side effects



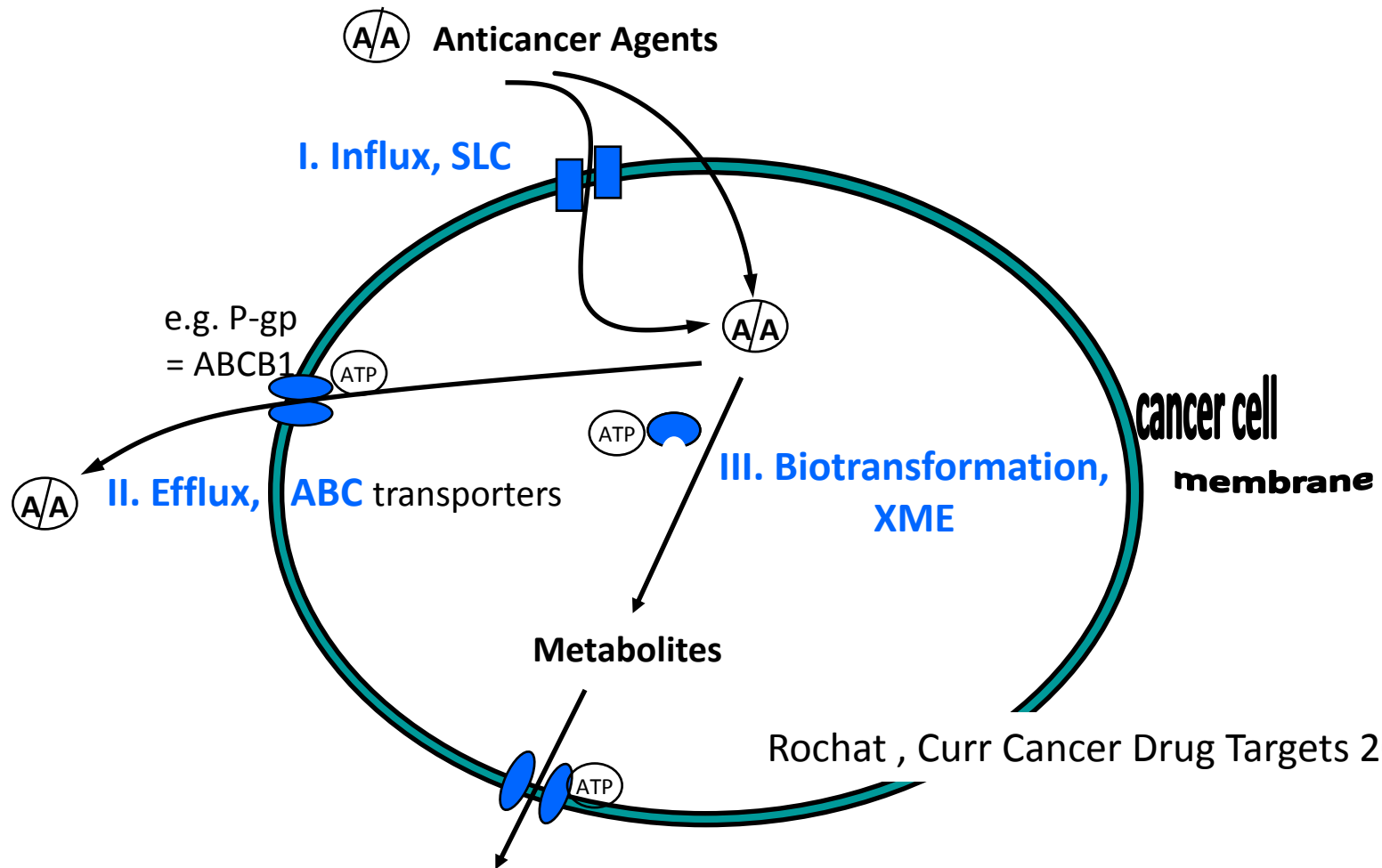
Widmer N et al, Br J Cancer 2008

Total and free Imatinib



Widmer N et al, Br J Clin Pharmacol 2006

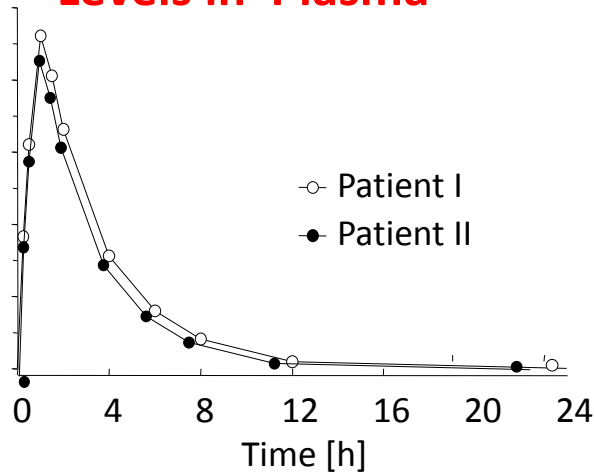
ADME players at cellular level



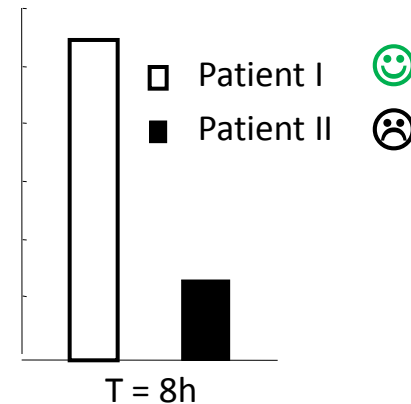
Rochat , Curr Cancer Drug Targets 2009

Rule #1 in ADME :

Levels in Plasma



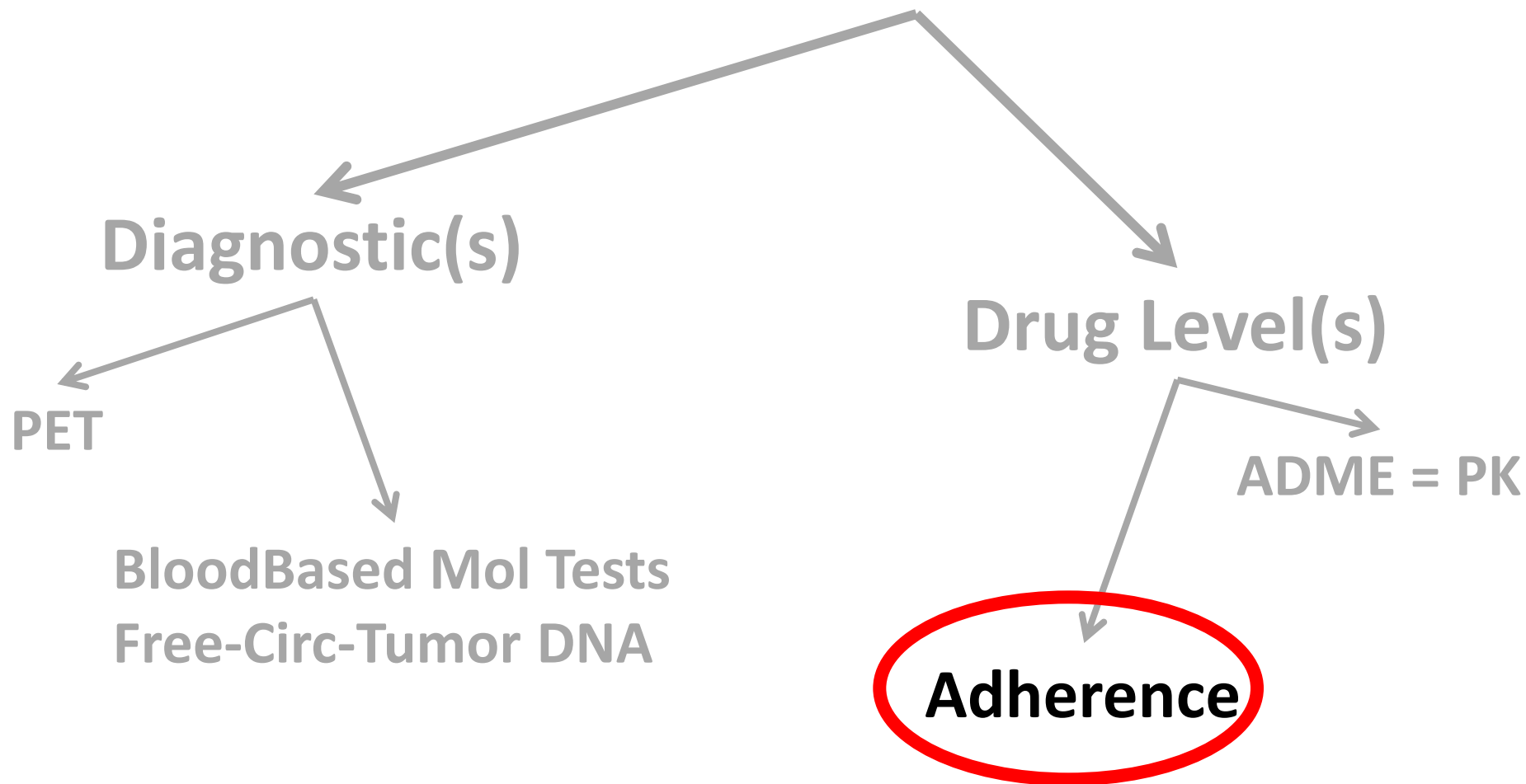
Levels in Tumors



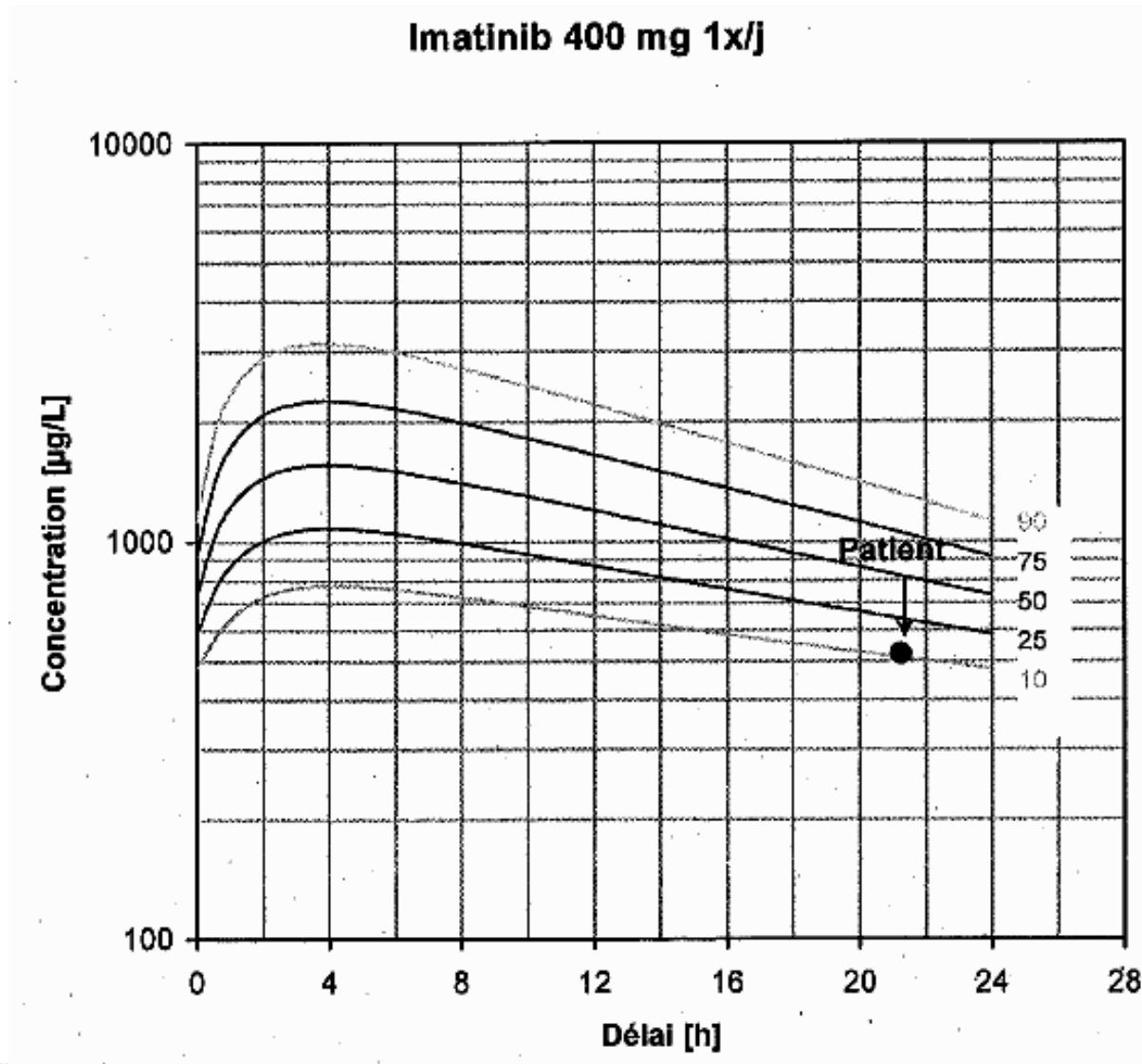
Blood PK is different from **intratumoral** PK

Rochat , Curr Cancer Drug Targets 2009

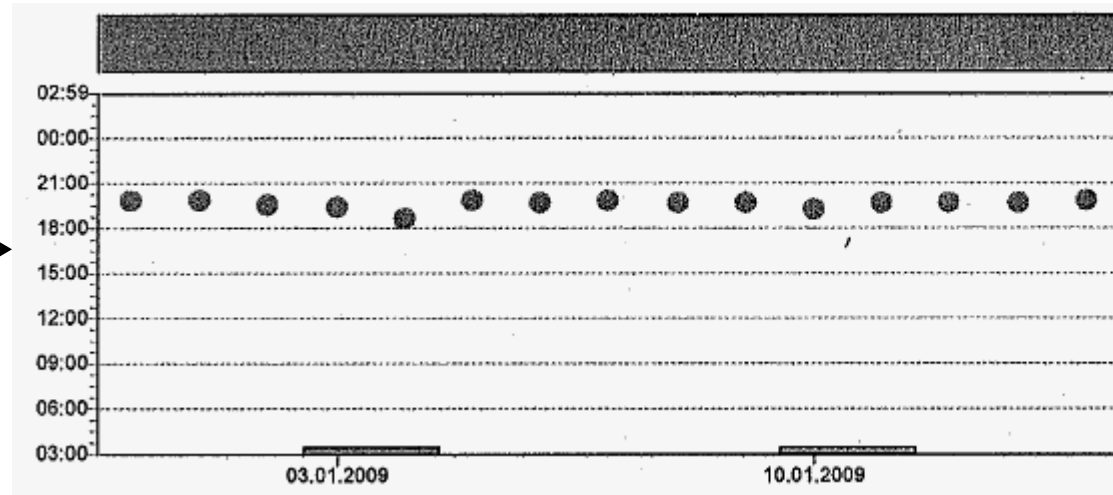
Personalising → Outcome



Progression ?



Adherence = Execution X Persistence



Montemurro, CHUV, Lausanne

Electronic „Pill Box“

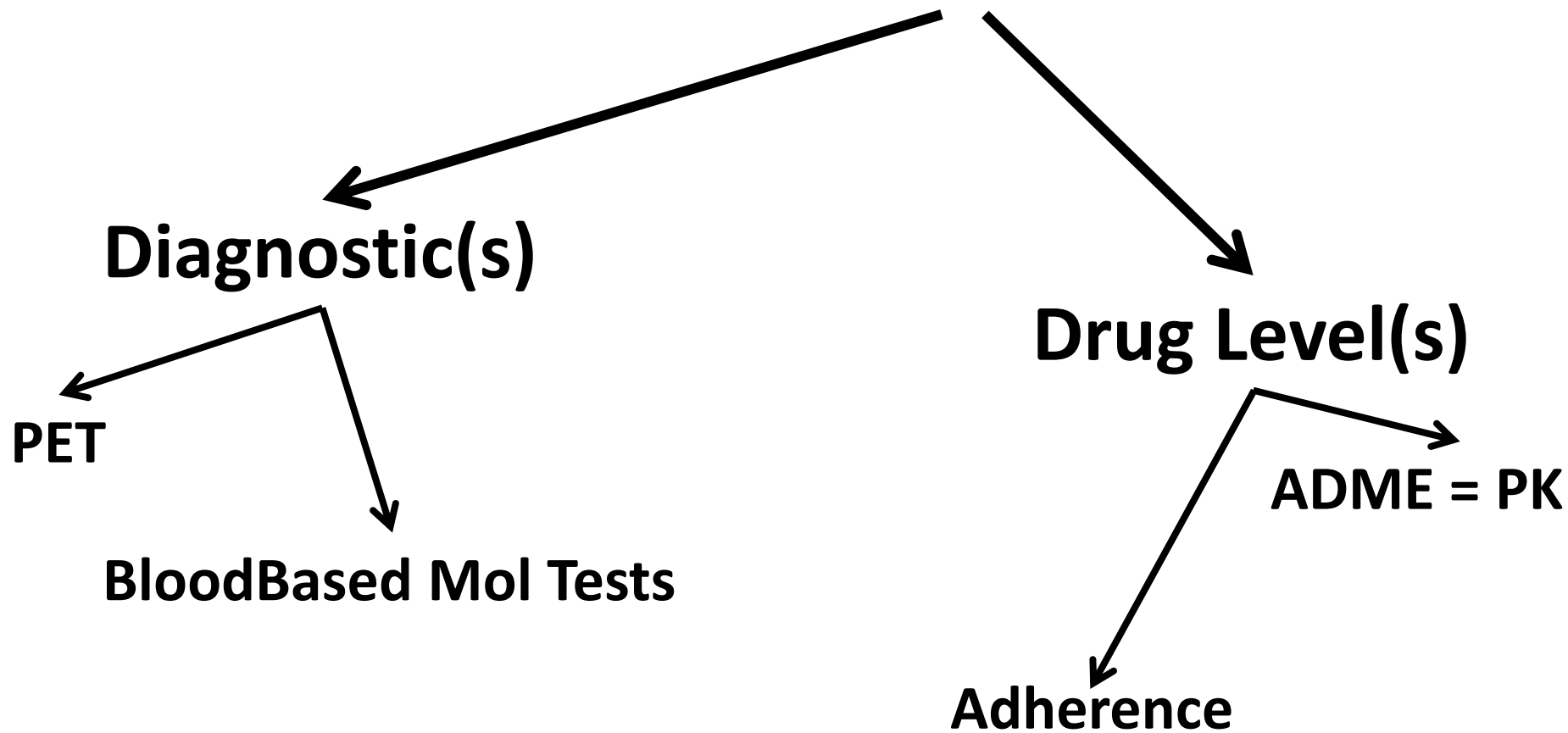
Jeanneret et al. Rev Med Suisse 2011

Adherence / Drug Levels

- **Drug Level(s)**
 - Probable Correlation with Outcome and Toxicity
 - Suggested Trough level > 1100ng/ml
- **Adherence**
 - Always double-check
 - Unreliable: Refill / Diary
 - Electronic «Pill Box»
 - Intervention / Education in patients «at risk»

Demetri et al, JCO 2009; Widmer et al Br J Cancer 2008; Call et al J Gastroint Cancer 2010
Jeanneret et al Rev Med Suisse 2011, Mathes et al CTR 2014, Blay et Rutkowski CTR 2014

Personalising → Outcome



Personalising medical therapy on the rest

Michael Montemurro