

Les « Highlights » de l'année d'un ASH à un autre ...

LMC

Vendredi 5 octobre 2018

Dr Quittet

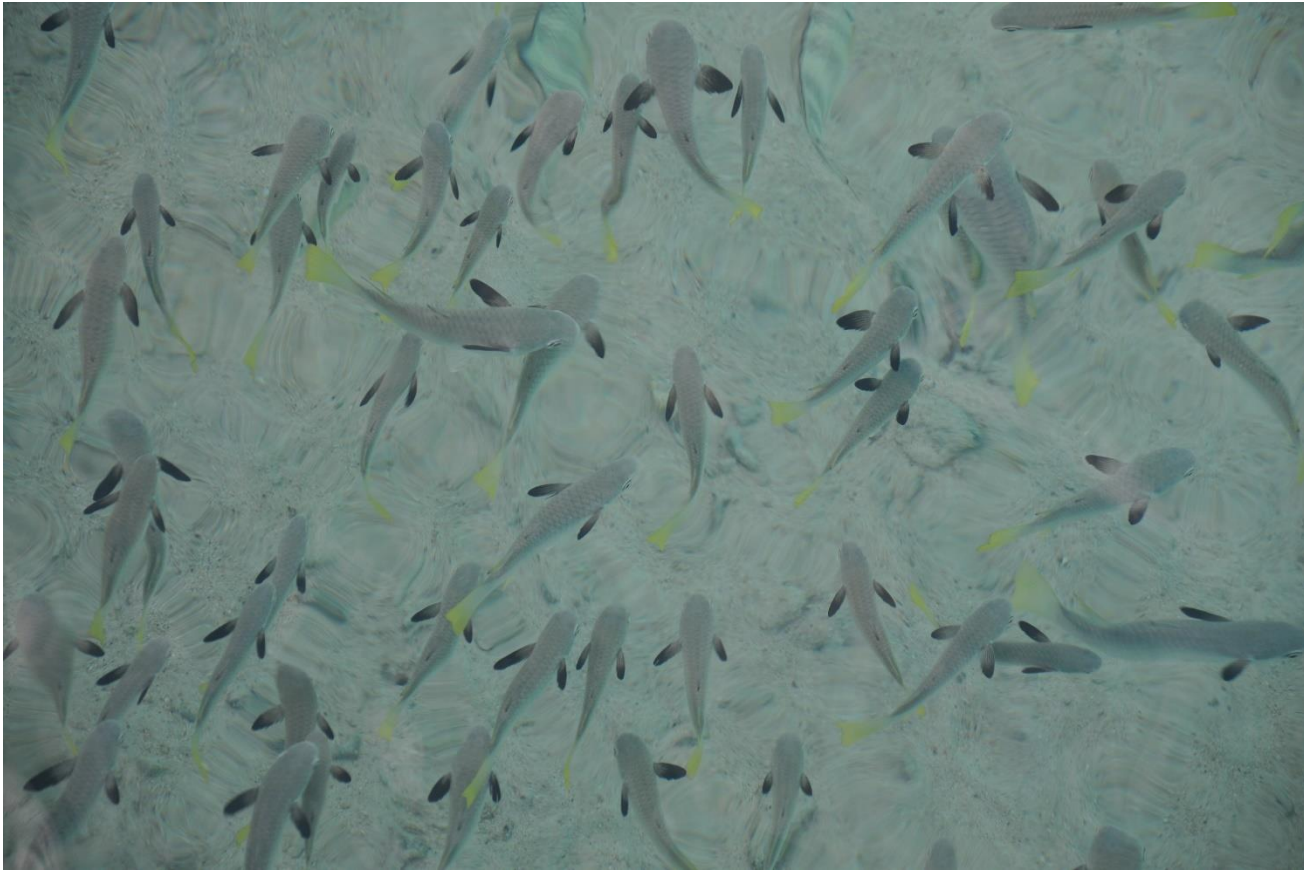
Réflexions sur la LMC en 2018: motivations +++ vacances à Tahiti



Actualités LMC 2018

- Actualité peu riche
 - Surtout axée encore sur le TFR (Treatment free remission)
 - ITK concernés: 2^{ème} génération

Neurones en actions !



TFR: considérations patients- médecins

- Patients éligibles ?
 - LMC-PC au diagnostic (of course !)
 - Pas d'expérience de résistance à quelconque ITK
 - RM profonde pendant 2 ans (RM 4,5)
 - Patients MOTIVÉS +++ et sans pression médicale !!!
 - Patients ayant compris que perte réponse n'est pas un échec
 - Patients se soumettent à suivi régulier même sans traitement
- Au total environ 31% sont éligibles (en 1^{ère} ligne ITK)



Quelques rappels sur TFR

- Nombreux essais dans le passé
 - ont validé le TFR: Imatinib +++
 - TFR peut être proposé en dehors d'essai thérapeutique
 - TFR est un des objectifs des traitements ITK !
- AMM du Nilotinib
 - Etude Enest Freedom
- Autres TFR ITK2



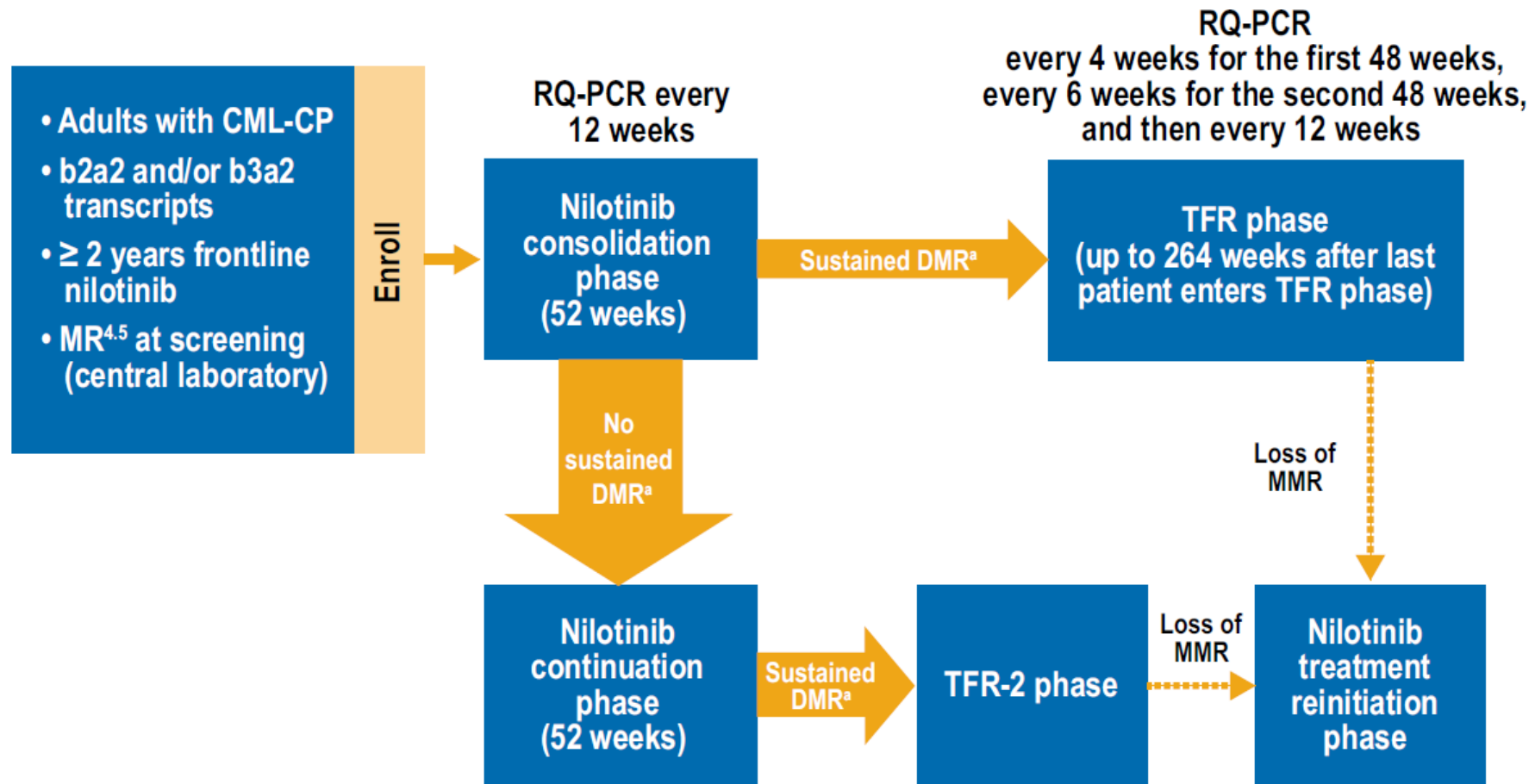
Après mures réflexions



Etude Enest Freedom

- STOP Nilotinib en 1^{ère} ligne

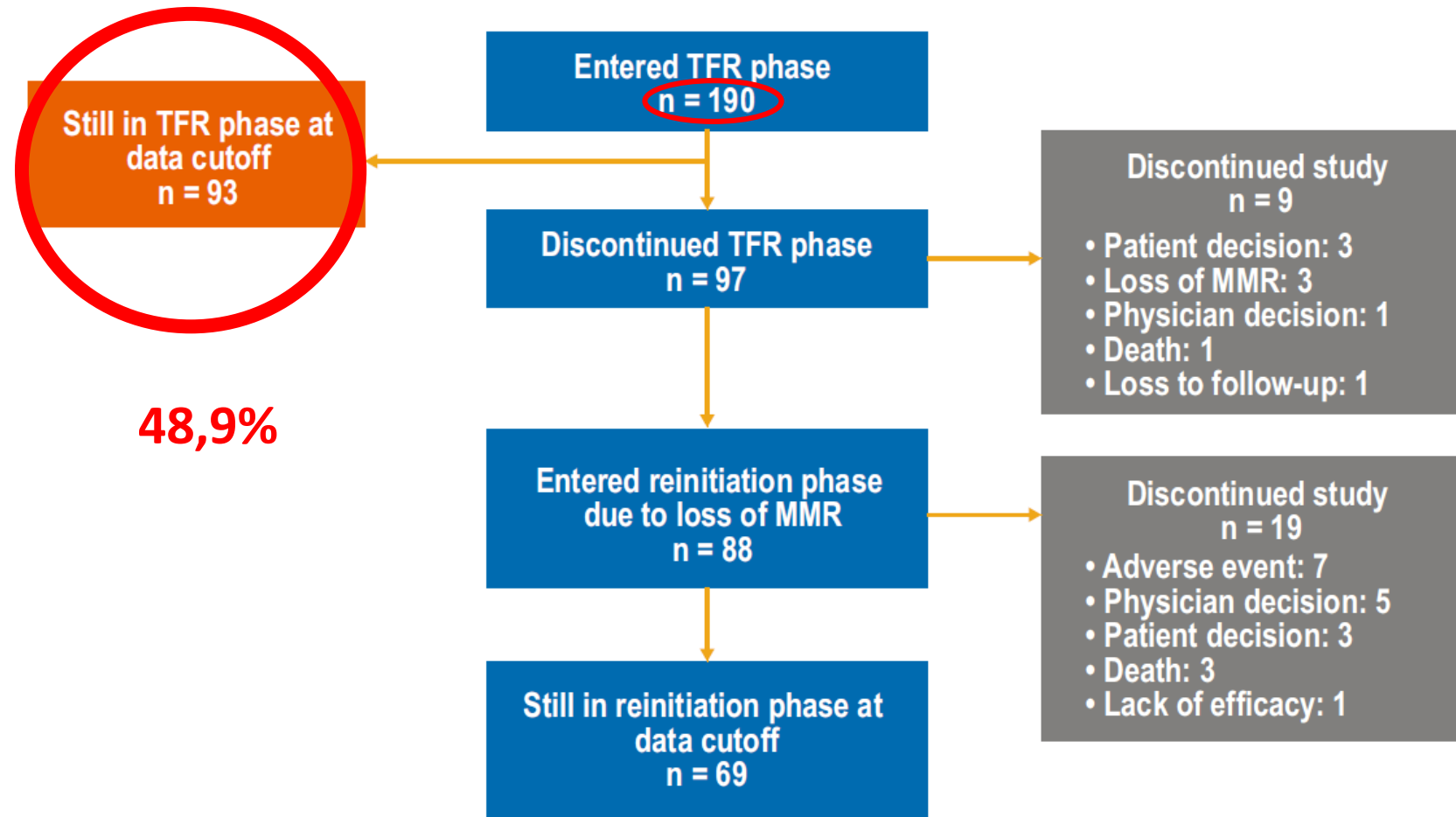
Enest freedom



Etude Enest Freedom

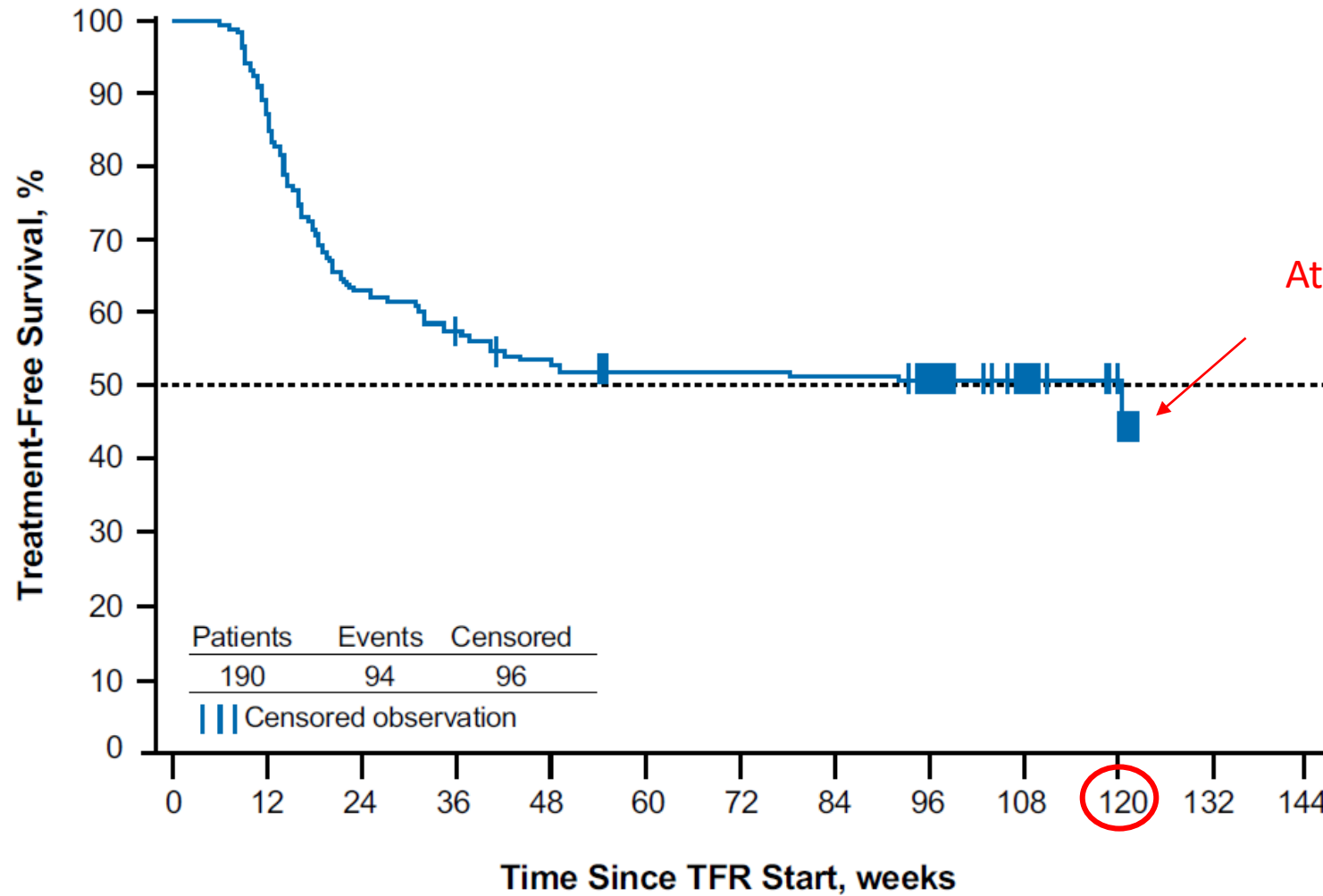
- Update à 96 semaines
 - TFR
 - TFS
 - Données sur réintroduction du Nilotinib

Enest Freedom: TFR à 96 semaines



TFS Enest Freedom

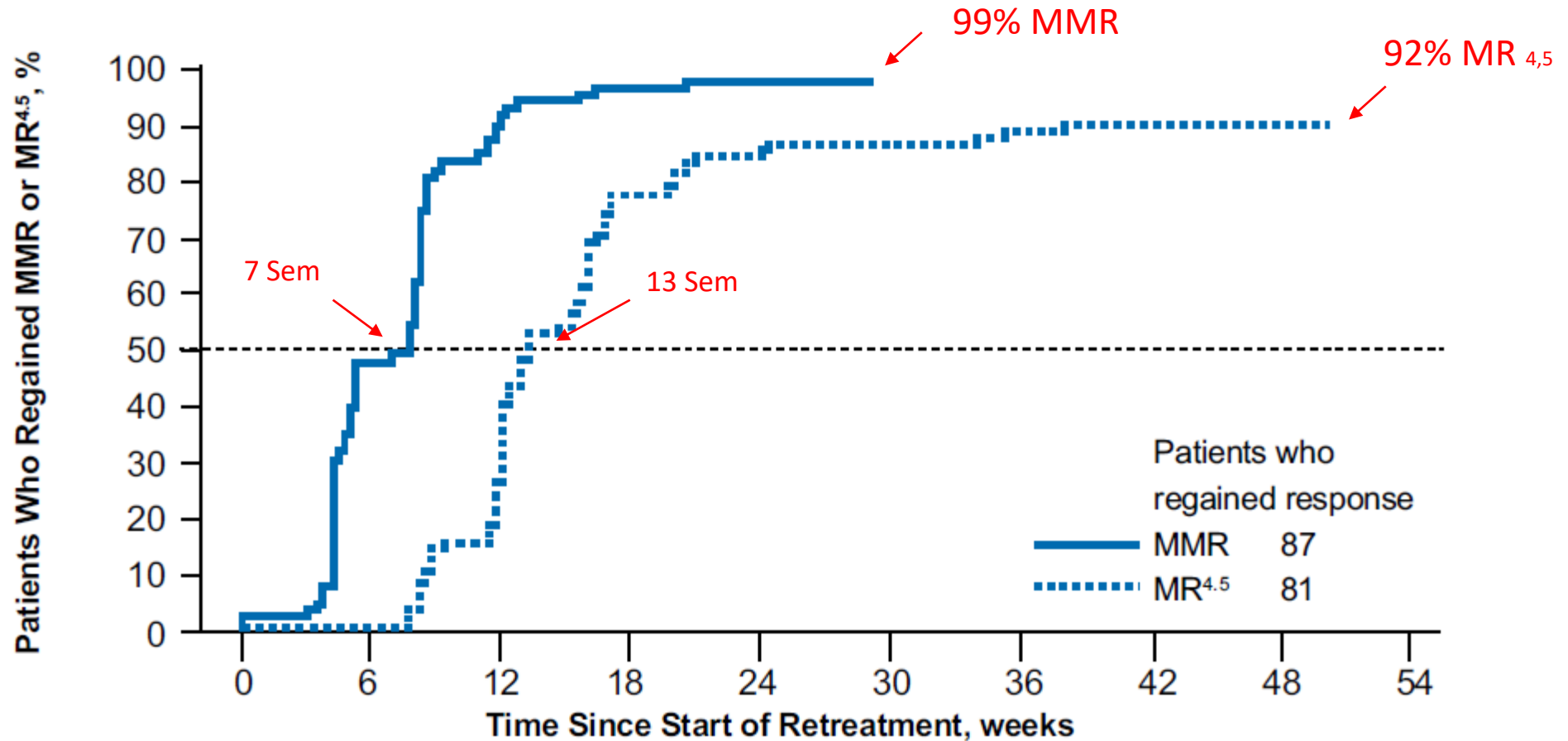
TFS: perte de MMR
Réintroduction Nilotinib
PROG: AC/BC
Décès



Enest Freedom: Facteurs associés à TFR

TFR rate, n/N (% [95% CI])	TFR population ($n = 190$)	
	48 weeks	96 weeks
Sokal risk score at diagnosis		
Low	39/62 (62.9 [49.7–74.8])	38/62 (61.3 [48.1–73.4])
Intermediate	25/50 (50.0 [35.5–64.5])	25/50 (50.0 [35.5–64.5])
High	9/28 (32.1 [15.9–52.4])	8/28 (28.6 [13.2–48.7])
Unknown	25/50 (50.0 [35.5–64.5])	22/50 (44.0 [30.0–58.7])
<i>BCR-ABL</i> ^{IS} level in the consolidation phase		
MR ^{4.5} in all assessments	90/170 (52.9 [45.2–60.6])	86/170 (50.6 [42.8–58.3])
≥ 1 assessment of MR ⁴ but not MR ^{4.5}	8/20 (40.0 [19.1–63.9])	7/20 (35.0 [15.4–59.2])
<i>MR</i> ⁴ <i>BCR-ABL</i> on the International Scale (<i>BCR-ABL</i> ^{IS}) ≤ 0.01%, <i>MR</i> ^{4.5} <i>BCR-ABL</i> ^{IS} ≤ 0.0032%, TFR treatment-free remission		

Réponses après réintroduction Nilotinib



AEs pendant Enest Freedom

Syndrome sevrage des ITKs

Patients, <i>n</i> (%)	Consolidation phase (<i>n</i> = 100)	TFR phase	
		First 48 weeks (<i>n</i> = 100)	Second 48 weeks (<i>n</i> = 100)
Cardiovascular events	3 (3.0)	2 (2.0)	1 (1.0)
Ischemic cerebrovascular events	1 (1.0)	1 (1.0)	0
Ischemic heart disease	1 (1.0)	0	1 (1.0)
Peripheral arterial occlusive disease	1 (1.0)	1 (1.0)	0
Musculoskeletal pain +++	17 (17.0)	34 (34.0)	9 (9.0)
Fluid retention	3 (3.0)	4 (4.0)	4 (4.0)
Edema and other fluid retentions	2 (2.0)	3 (3.0)	4 (4.0)
Severe	1 (1.0)	1 (1.0)	0
Hepatotoxicity	2 (2.0)	2 (2.0)	0
Cardiac failure	0	1 (1.0)	0
Rash	5 (5.0)	1 (1.0)	1 (1.0)
Myelosuppression (thrombocytopenia)	1 (1.0)	0	0
Pancreatitis	1 (1.0)	0	0
Significant bleeding	0	0	1 (1.0)
Gastrointestinal hemorrhage	0	0	1 (1.0)

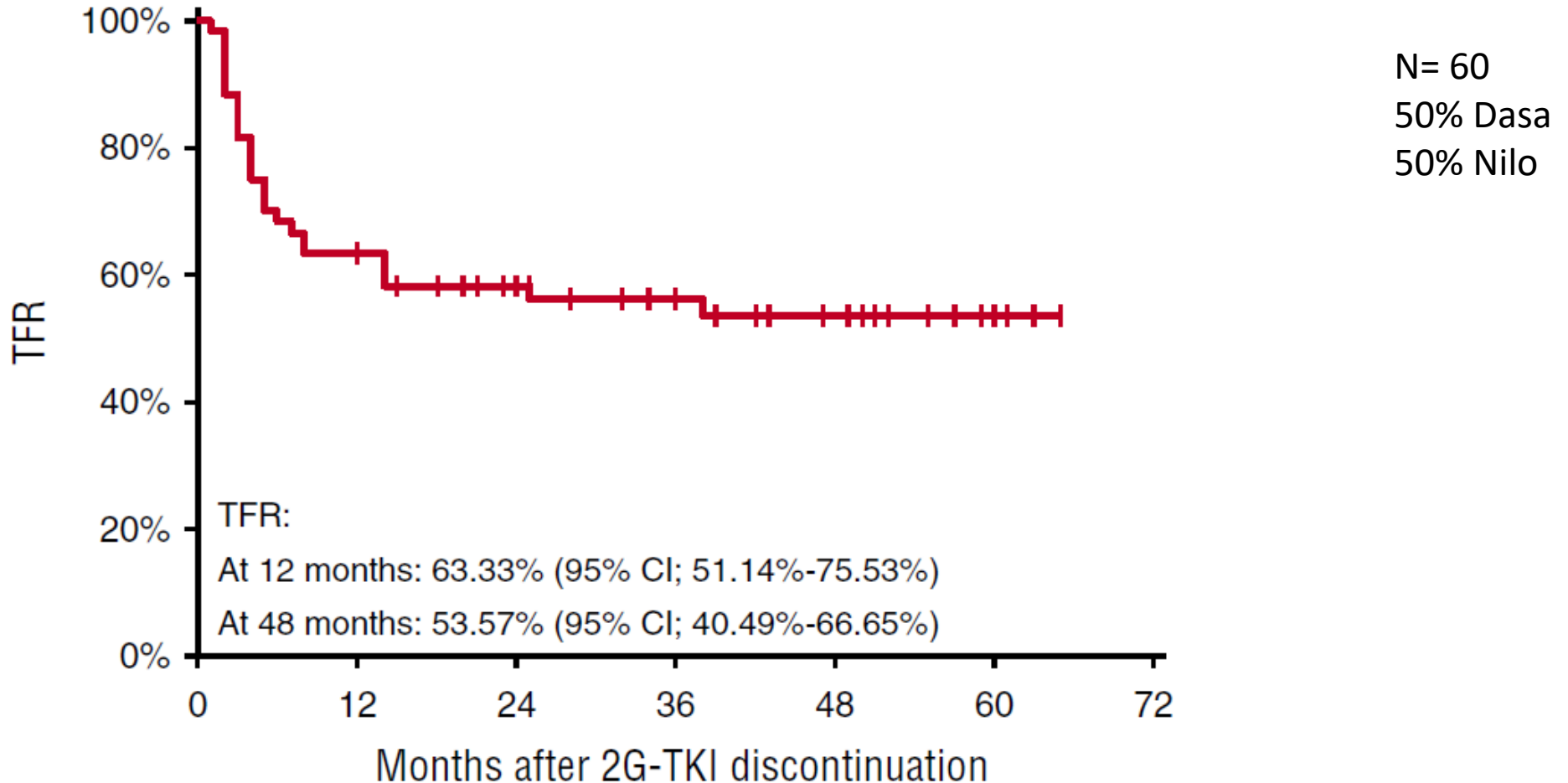
Décès Enest Freedom

Deaths, <i>n</i> (%)	Consolidation phase (<i>N</i> = 215)	TFR phase (<i>n</i> = 190)	Reinitiation phase (<i>n</i> = 88)	Post-treatment follow-up ^b
Total	2 (0.9)	1 (0.5)	3 (3.4)	2
Cardiac arrest	1 (0.5)	0	0	0
Suicide	1 (0.5)	0	0	0
Acute myocardial infarction	0	0	1 (1.1)	0
Respiratory failure	0	0	1 (1.1) ^c	0
Other cancers	0	0	0	2 ^{b,c}
Unknown cause	0	1 (0.5)	1 (1.1)	0

Eclaircissements sur autres ITK



STOP ITK2: patients en 1^{ère} à 3^{ème} d'ITK2



Revue 2018: TFR

Rappel des études STOP Imatinib

Table 1 Overview of imatinib discontinuation studies

Study	Nb	TKI treatment	Duration of TKI treatment prior to discontinuation	Depth and duration of response prior to discontinuation	Molecular relapse and trigger to resume TKI
STIM	100	Imatinib 1st line or after IFN- α	At least 3 years	MR4.5 with undetectable <i>BCR-ABL1</i> transcripts for at least 2 years	Loss of MMR or increase in <i>BCR-ABL1</i> ≥ 1 log
TWISTER	40	Imatinib 1st line or after IFN- α	At least 3 years	MR4.5 with undetectable <i>BCR-ABL1</i> transcripts for at least 2 years	Loss of MMR or confirmed loss of MR4.5
A-STIM	80	Imatinib 1st line or after IFN- α	At least 3 years	MR4.5 for at least 2 years	Loss of MMR
KIDS	90	Imatinib 1st line or after IFN- α	At least 3 years	MR4.5 with undetectable <i>BCR-ABL1</i> transcripts for at least 2 years	Loss of MMR
ISAV	108	Imatinib 1st line or after IFN- α	At least 2 years	MR4 or MR4.5 with undetectable <i>BCR-ABL1</i> transcripts for at least 18 months	Loss of MMR
EURO-SKI	821	Imatinib 1st line or after IFN- α , dasatinib or nilotinib 1st or subsequent line, excluding patients with resistance to any TKI	At least 3 years	MR4 for at least 1 year	Loss of MMR

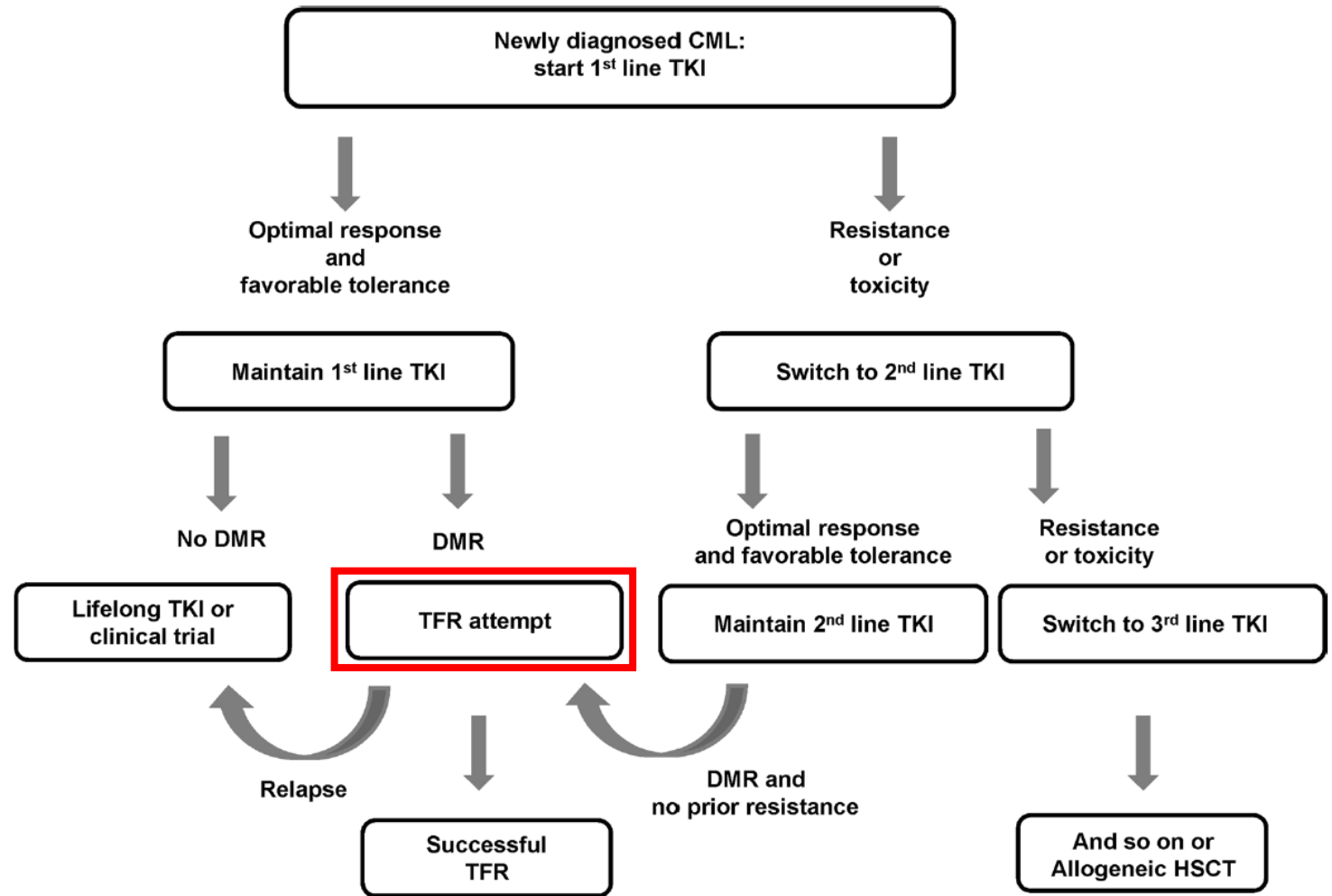
Revue 2018: TFR

Rappel des études STOP ITK2

Table 2 Overview of dasatinib or nilotinib discontinuation studies

Study	Nb in TFR phase	TKI treatment	Duration of TKI treatment prior to discontinuation	Depth and duration of response prior to discontinuation	Molecular relapse and trigger to resume TKI
DADI	63	Dasatinib 2st line or subsequent line	At least 1 year of dasatinib	MR4 for at least 1 year	Loss of MR4
DASFREE	84	Dasatinib 1st or subsequent line	At least 2 years	MR4.5 for at least 1 year + 3 additional months of MR4.5 confirmation	Loss of MMR
D-STOP	54	Dasatinib 1st or subsequent line	At least 2 years of dasatinib consolidation	MR4 with undetectable <i>BCR-ABL1</i> transcripts for at least 2 years	Confirmed loss of MR4
STOP 2G-TKI	100	Dasatinib or nilotinib 1st or subsequent line	At least 3 years	MR4.5 with undetectable <i>BCR-ABL1</i> transcripts for at least 2 years	Loss of MMR
STAT2	78	Nilotinib 2nd line	At least 2 years of nilotinib consolidation	MR4.5 for at least 2 years	Confirmed loss of MR4.5
NILSt	87	Nilotinib 1st or subsequent line	At least 2 years of nilotinib	MR4.5 for at least 2 years	Loss of MR4.5
ENESTop	126	Nilotinib 2nd line	At least 2 years + 1 additional year of nilotinib	MR4.5 for at least 1 year	Loss of MMR or confirmed loss of MR4
ENESTpath	Not yet available	Nilotinib 2nd line in the absence of MR4 during imatinib therapy	Nilotinib for 2 or 3 years	MR4 for at least 1 year	Loss of MMR or confirmed loss of MR4
ENESTfreedom	190	Nilotinib 1st line	At least 2 years + 1 additional year of nilotinib	MR4.5 for at least 1 year	Loss of MMR

Revue 2018: TFR



Conclusion: Qu'avez-vous retenu de cette présentation ?

