TFR – Take Home Messages

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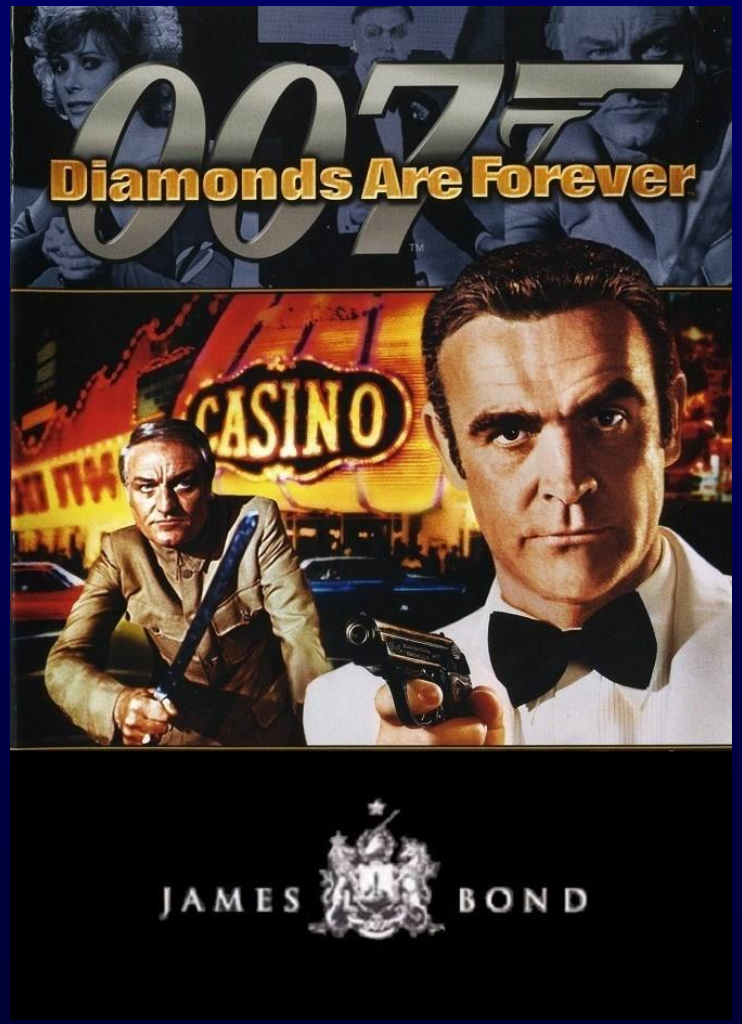
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(imatinib mesylate)
Tablets
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Rx only
Each tablet contains 100 mg of imatinib free base.
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SCEMBLIX®
(asciminib)
Tablets
40 mg
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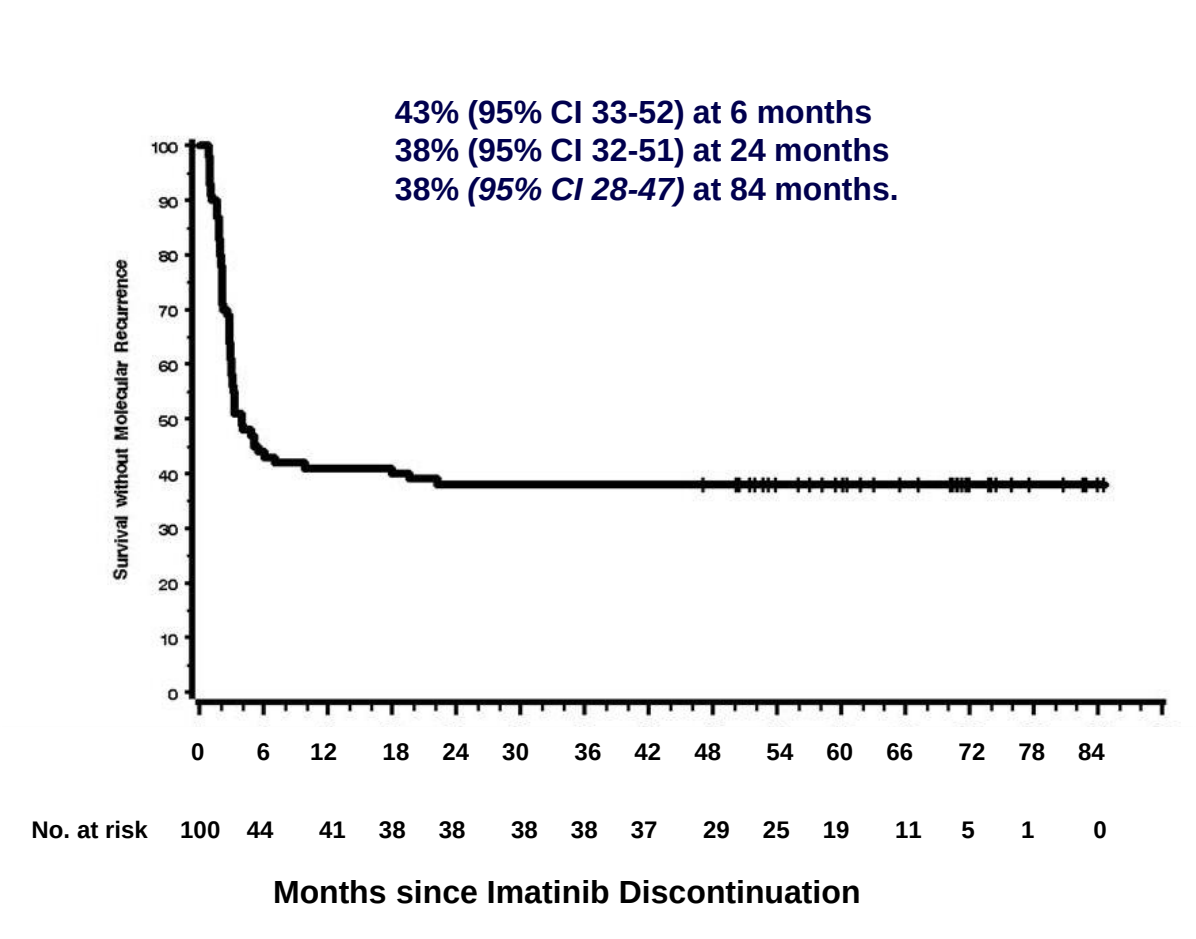
TKIs are not?

STIM - Molecular Recurrence-Free Survival



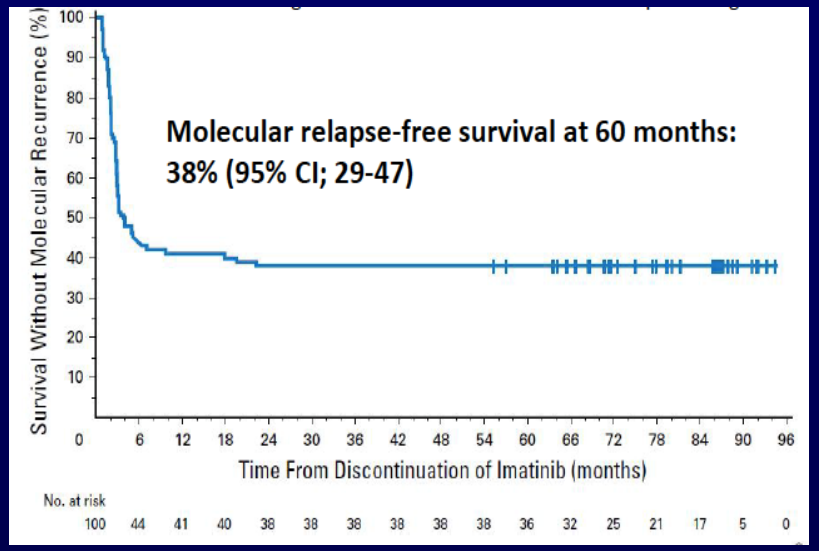
- Median follow-up 65 mo
- No-Recurrence 39 pts
  - 16 stable CMR
  - 23 intermittent positive
- Median time to recurrence (n=61) 2.5 mo
- 17 lost MMR
- 57 re-started Rx:
  - 55 re-gained CMR
- Predictors of recurrence: sex, Sokal

Mahon et al. Lancet Oncol 2010; 11: 1029-35; Etienne G, et al. Blood. 2015;126 [abstract 345].

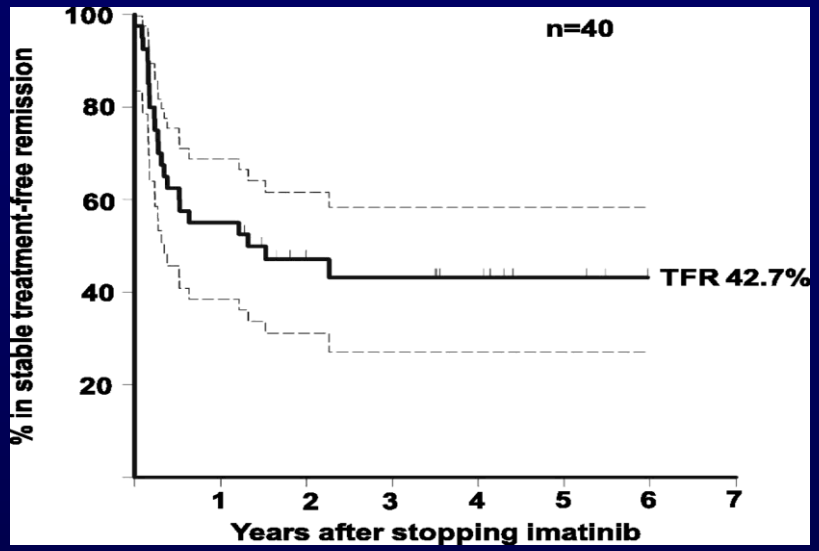
FOOD
B 865
JUNE 1, 2014

Treatment-Free Remission

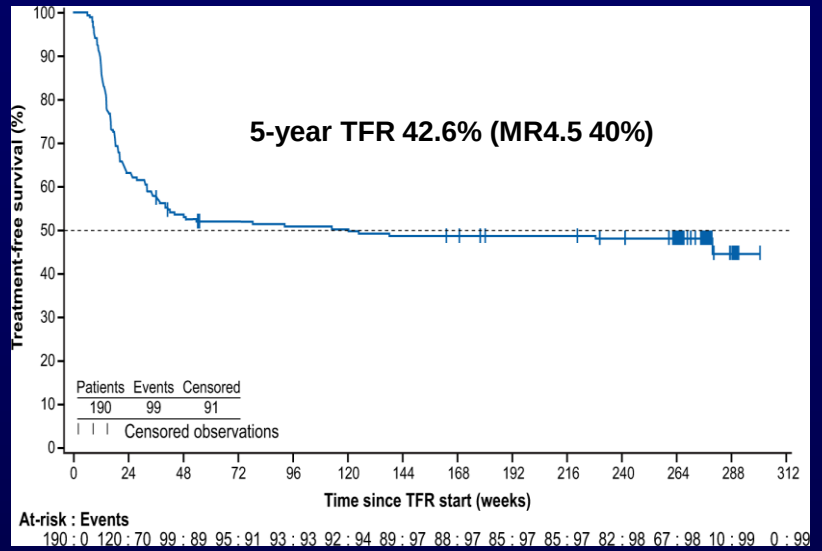
STIM[1]



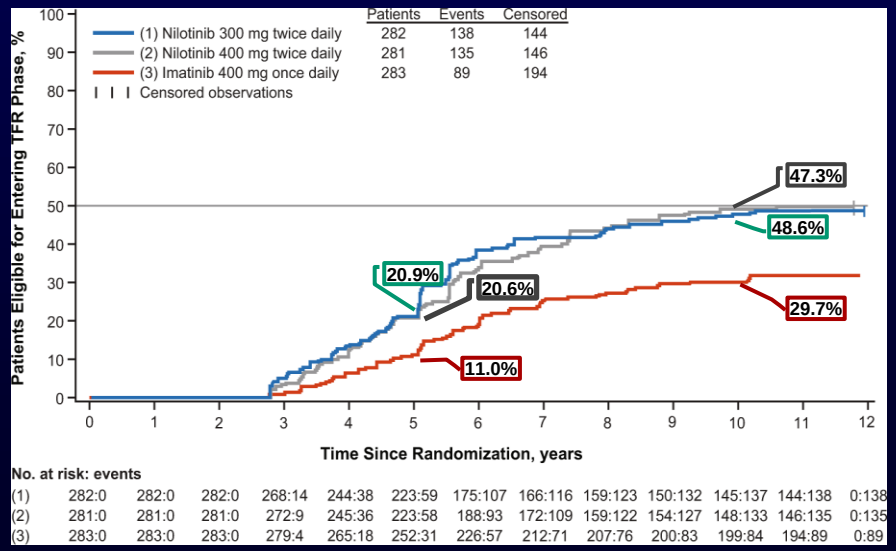
TWISTER[2]



ENESTfreedom[3]



ENESTnd[4]



BFORE[5]

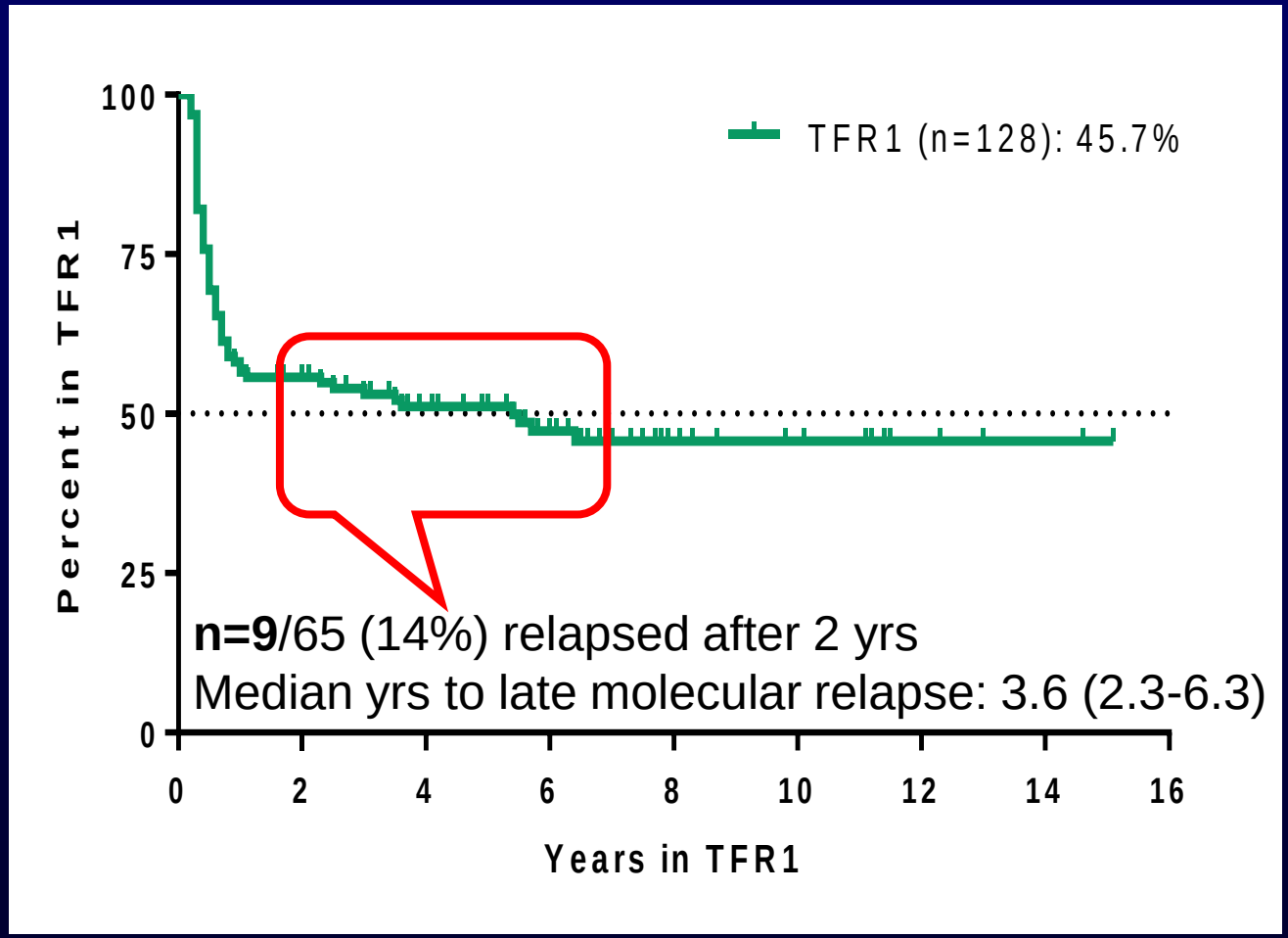
- 2-year sustained MR4: bosutinib 32.5% vs imatinib 26.5% (OR 1.33 [95% CI, 0.92, 1.93])

~47% eligible
X
~60% TFR
~28% Success

[1]Etienne et al. JCO 2017; 35: 298-305; [2]Ross et al. Blood 2013; 122: 515-22; [3]Radich et al. Leukemia 2021; 35: 1344-55; [4]Kantarjian et al. Leukemia 2021; 35: 440-53; [5]Brümmendorf TH, et al. *Blood.* 2020;136(Suppl 1): Abstract 46

Treatment-Free Remission
Single Institution Experience Over 15 Years

- Observational study of patients who discontinued TKI after achieving deep molecular response (≥ MR4)
- N = 128 in TFR1
- Median follow-up in TFR1: 6.5 y
- Median TKI duration: 7.1 y
- TKI: frontline imatinib 61%, frontline 2G 11%, 2nd line 2G 28%
- MR4 100%, stable MR4 81%, stable MR4.5 67%
- MVA TFR duration: TKI duration, MR4 duration

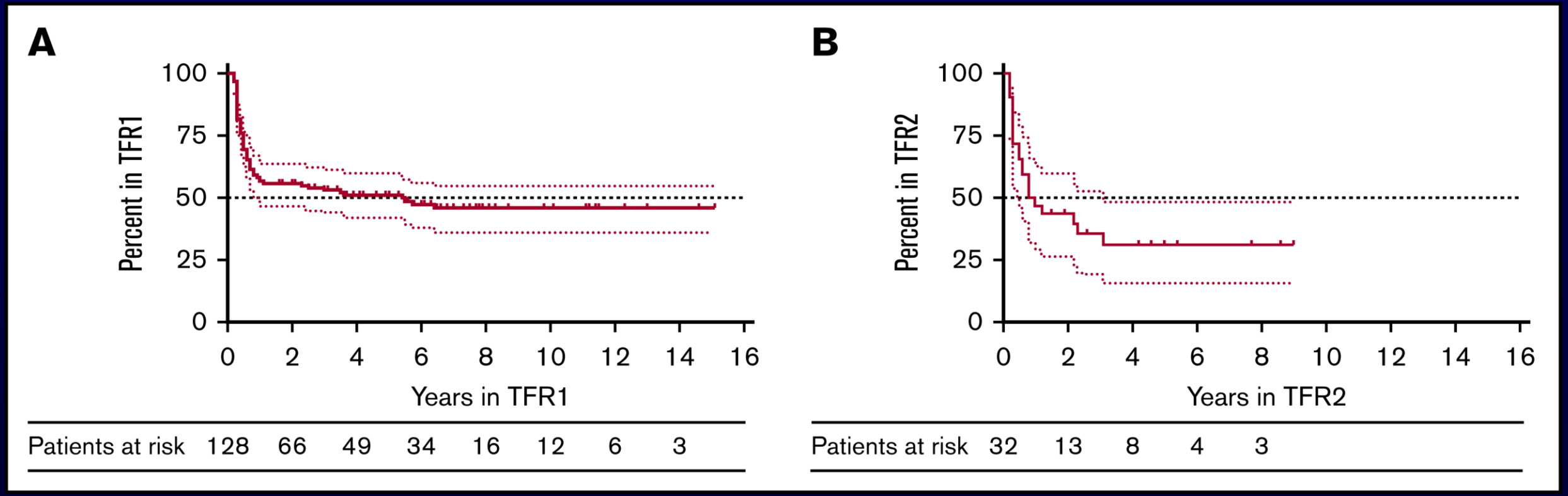


Rousselot P, et al. ASH 2019. Abstract 27.

Treatment-Free Remission - Second Attempt

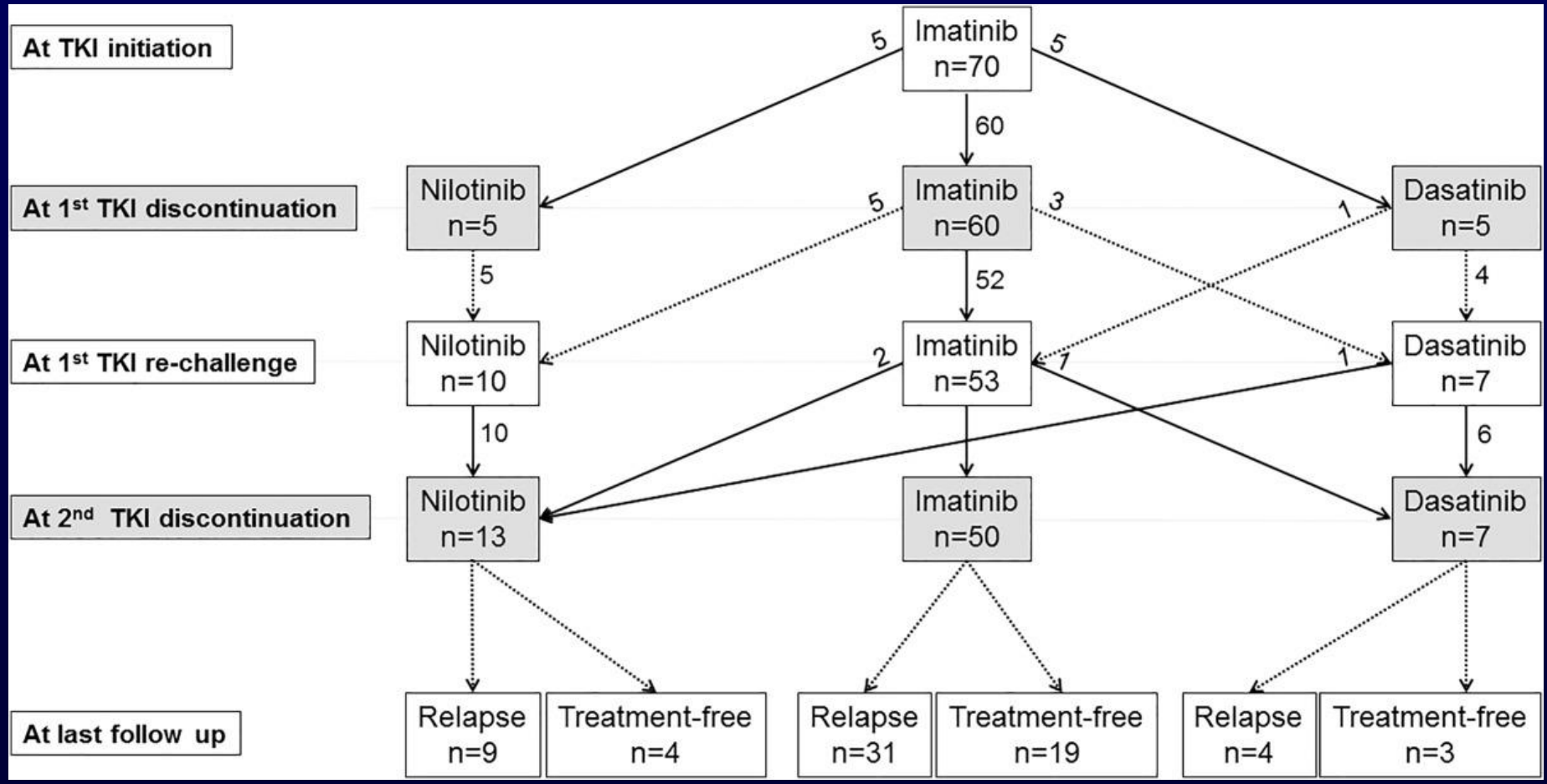
TFR 1st Attempt (N=128)

TFR 2nd Attempt (N=32)



Rousselot P, et al. ASH 2019. Abstract 27.

Second TFR Attempt



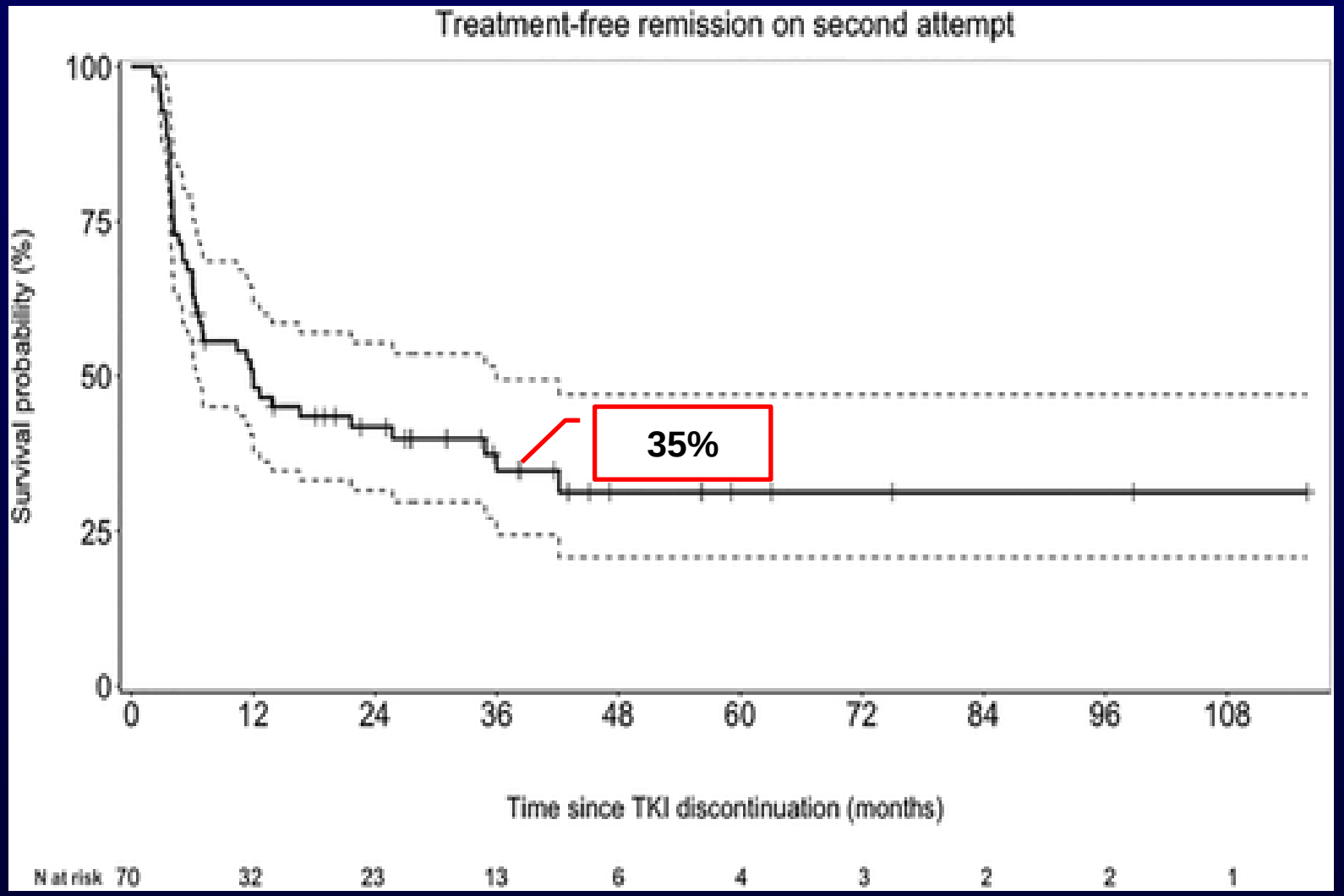
Legros et al. Cancer 2017; 123: 4403-10

2nd TKI Discontinuation - FiLMC

- 70 pts who failed 1st attempt at TKI discontinuation
- Median time from TKI resumption to 2nd TKI discontinuation 32 mo [6-72 mo]
- Median duration uMR4.5 prior to 2nd attempt: 25 mo [4-68 mo]
- Median F/U: 38 mo [5-117]
- No transformation AP/BP
- No predictive factors
- 25 pts in TFR (12 $UMD^{4.5}$)
- 45 lost MMR (44 re-challenged)
  - TKI free: 5 mo [2-42 mo]
  - 17 pts switched TKI at re-challenge
  - 34 pts regained $UMD^{4.5}$, 8 MMR

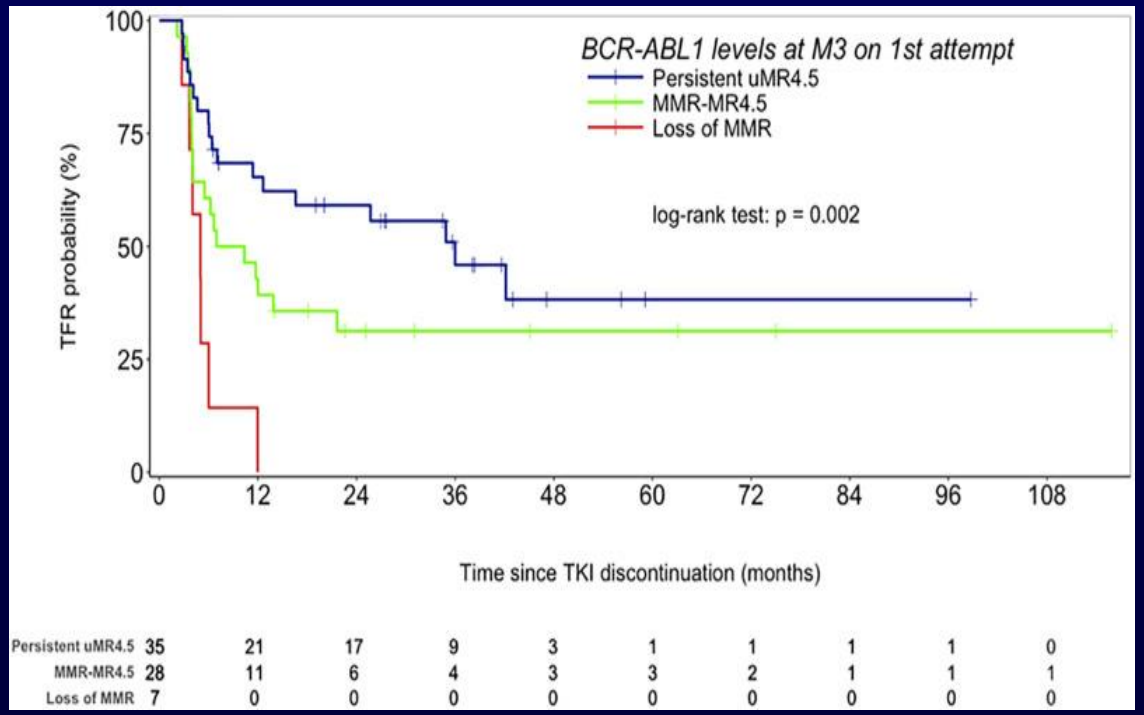
Legros et al. Cancer 2017; 123: 4403-10

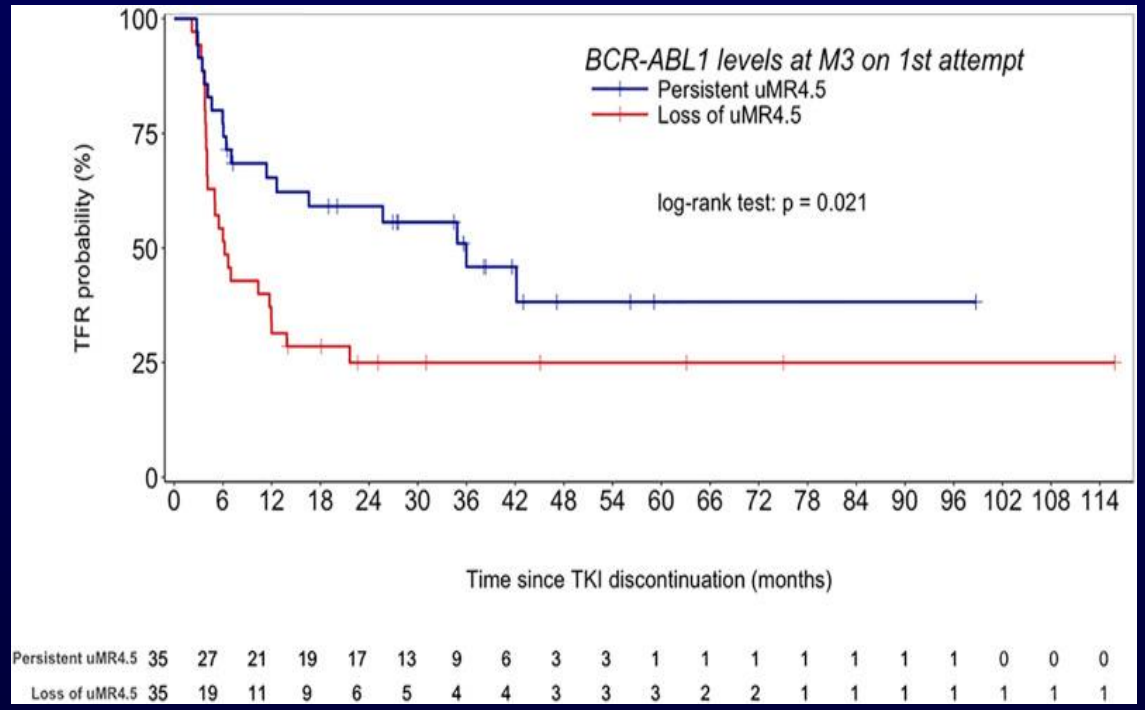
2nd TKI Discontinuation - FiLMC



Legros et al. Cancer 2017; 123: 4403-10

Second TFR Attempt by Molecular Status 3 Months After 1st Attempt





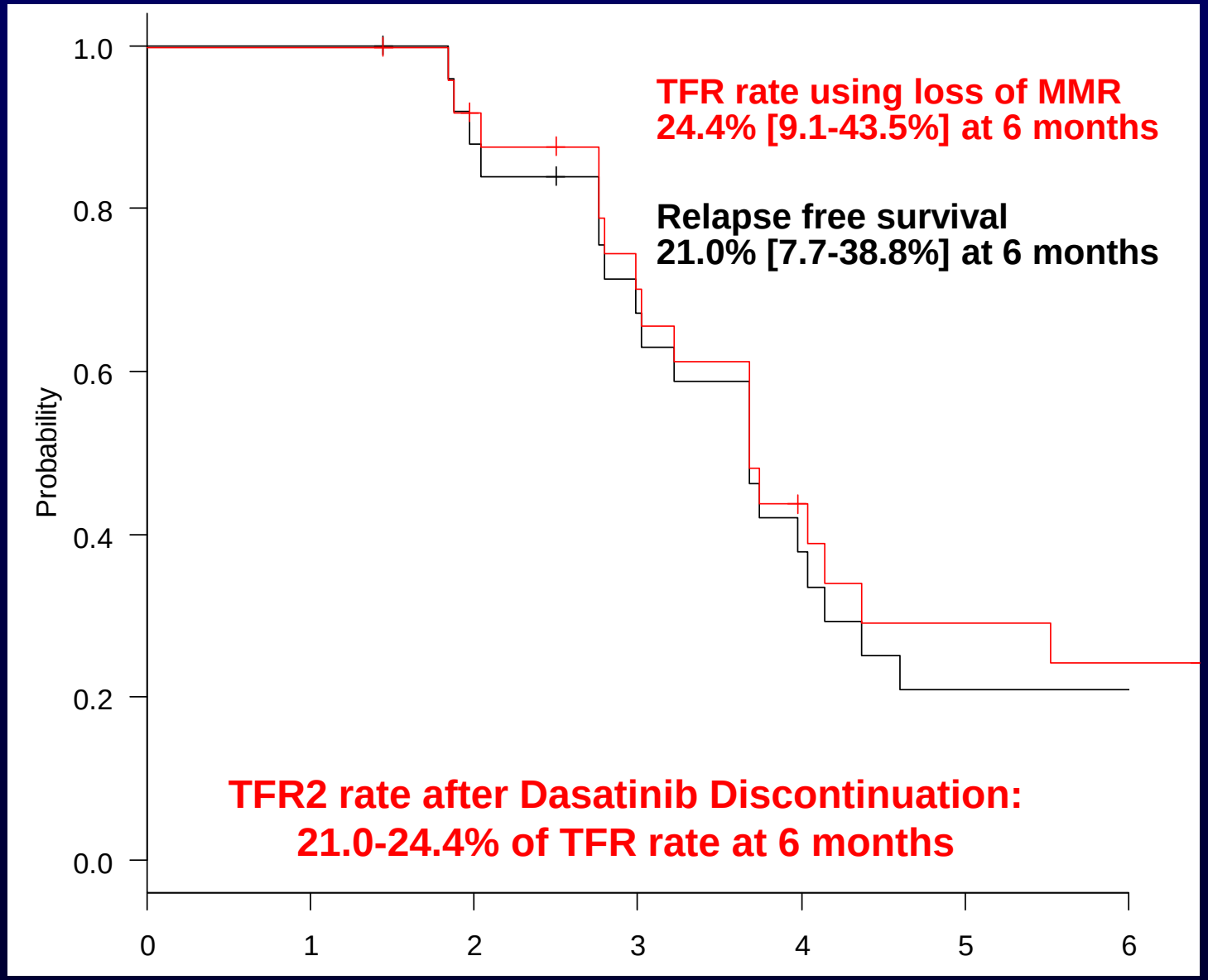
Legros et al. Cancer 2017; 123: 4403-10

TFR2 after Dasatinib Discontinuation - TRAD

- 51/53 patients who lost response after imatinib discontinuation received dasatinib
  - Eligible for discontinuation with MR4.5 ≥12 mo
- At 3 mo: MMR 98%, MR4 90%, and MR4.5 85%
- 25/51 (49%) patients attained MR4.5 for ≥12 mo and discontinued dasatinib for a 2nd TFR attempt (TFR2)
  - 21 still on dasatinib with MR4.5 for <12 months
- TFR2 rate after dasatinib discontinuation: 21/25 (84%) lost molecular response at a median of 3.7 months
- Estimated TFR2 rate after dasatinib discontinuation: 21.5±8.5% at 6 months (95% CI [7.9-39.5%])

Kim et al. ASH 2018; abstract #787

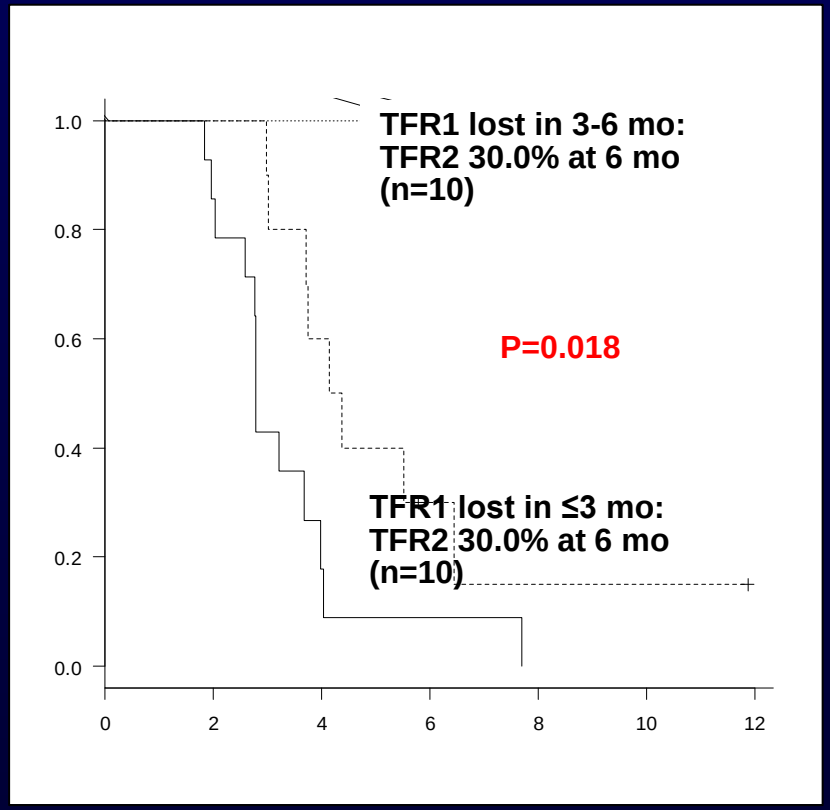
TRAD - TFR2 After Dasatinib Discontinuation



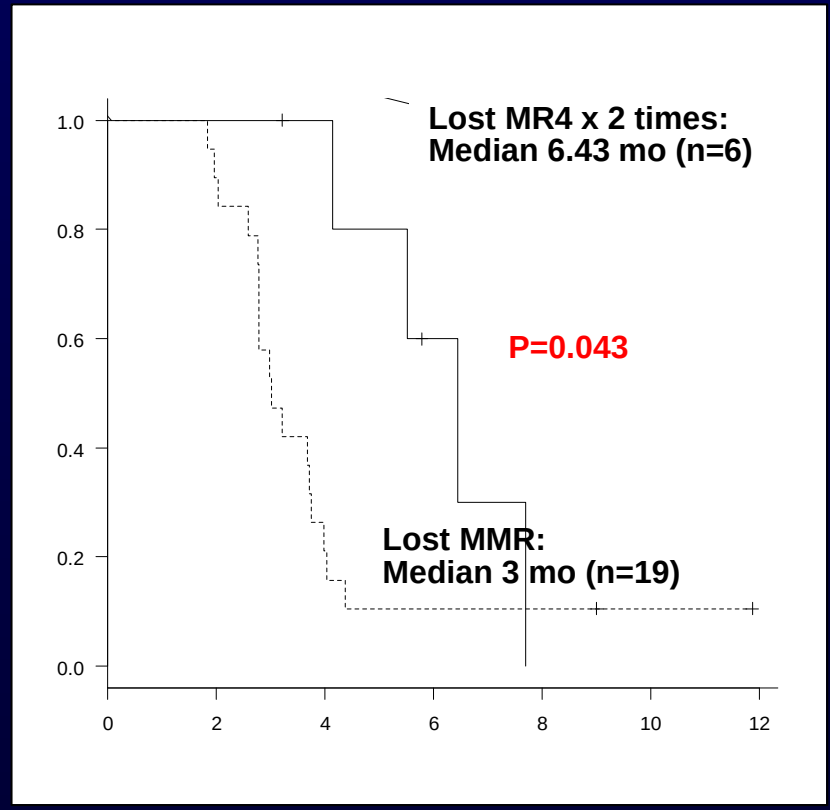
Kim et al. ASH 2018; abstract #787

Risk factors for TFR2 after Dasatinib Stop

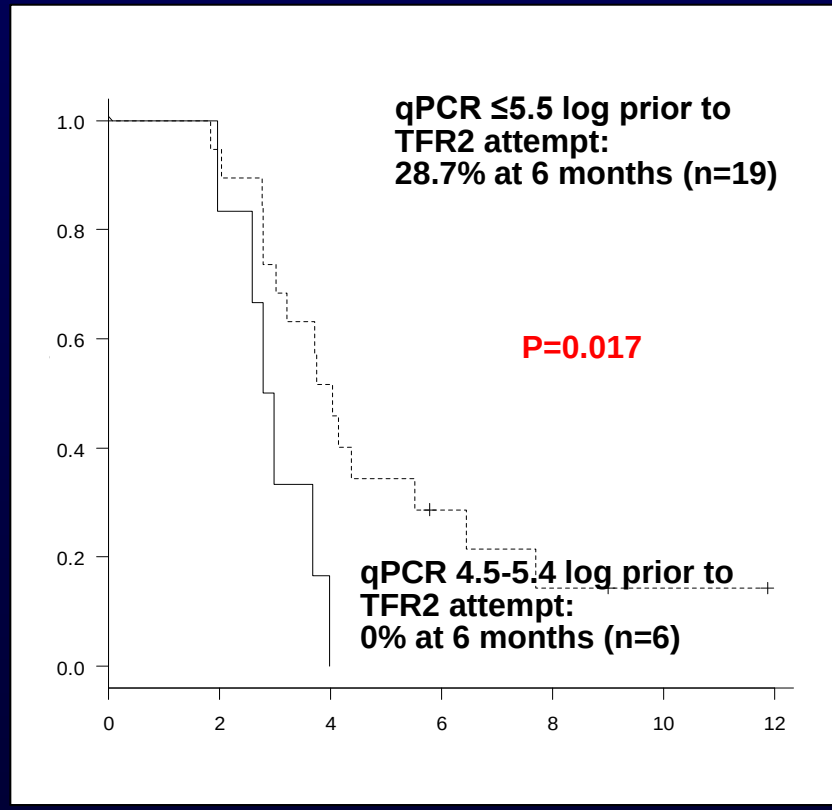
By TFR1 duration
(< 3 mo vs 3-6 mo vs >6 mo)*



By molecular relapse after TFR1
(loss of MMR loss vs loss of MR4 x2)



By BCR-ABL1 prior to TFR2 attempt
(≤5.5 log vs others)

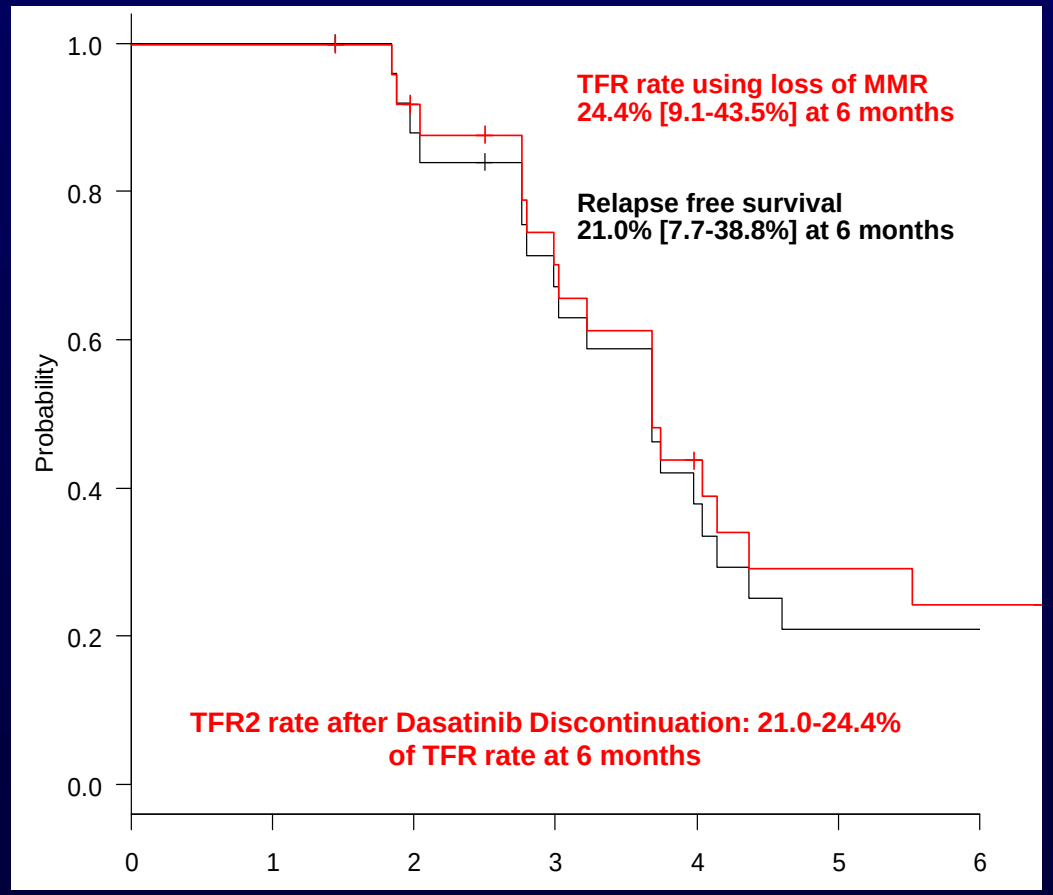


* The one patient who relapsed beyond 6 months of TFR1 did not lose molecular response after DA discontinuation

Kim et al. ASH 2018; abstract #787

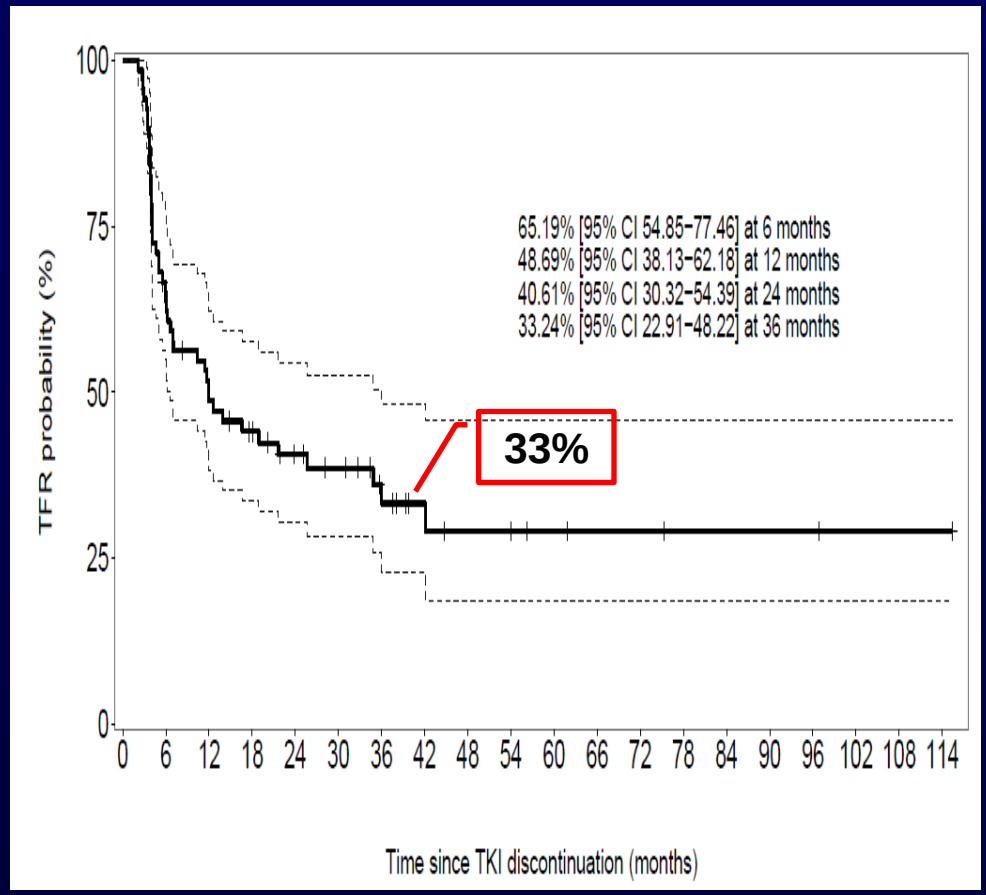
2nd Treatment Discontinuation Attempt

TRAD



- 1st attempt Imatinib, 2nd dasatinib
- Eligible 2nd attempt: MR4.5 ≥12 mo

FiLMC



- 1st attempt: imatinib 60, nilotinib 5, dasatinib 5
- 2nd attempt: imatinib 50, nilotinib 13, dasatinib 7
- Median duration MR4.5 before 2nd attept: 25 months (range, 4-68 months)

Kim et al. ASH 2018; abstract #787; Legros et al. Cancer 2017; 123: 4403-10

Second TKI Discontinuation

1st Attempt

2nd Attempt

53 pts

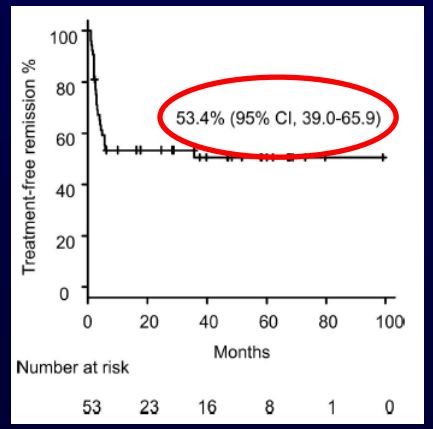
Success → 28 (53.4%)

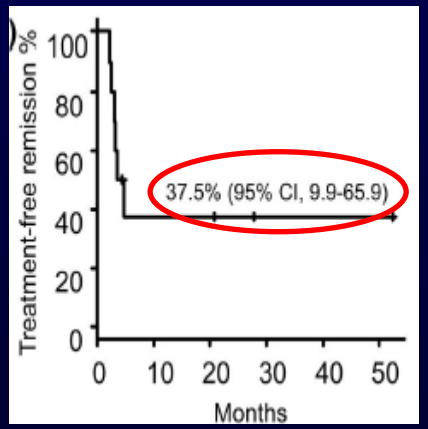
Relapse → 25 → 10

All 2GTKI

Success → 4 (37.5%)

Relapse → 6



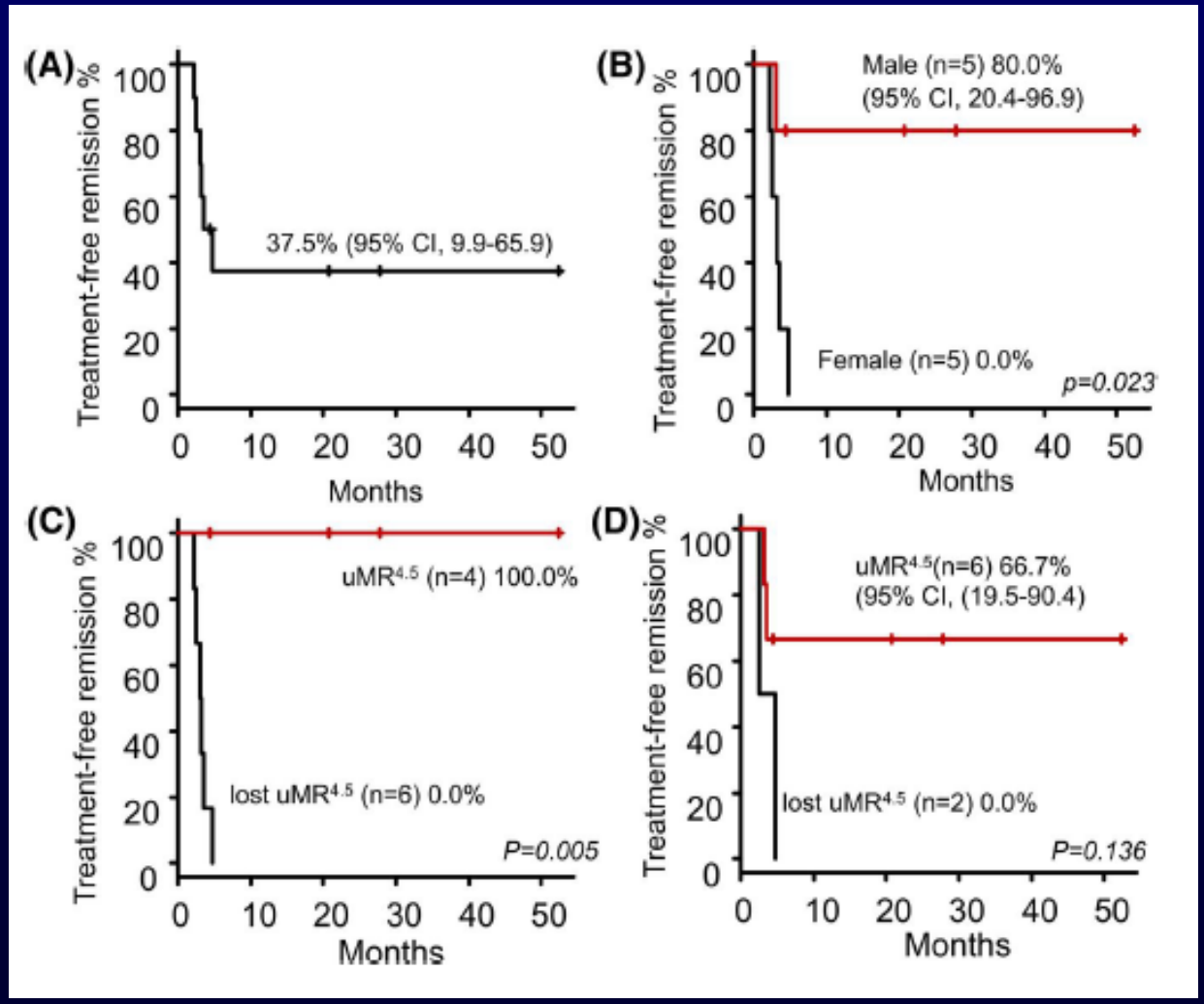


Ureshino et al. Hematol Oncol 2021; 39: 549-57

Second TFR Attempt

Overall

Sex

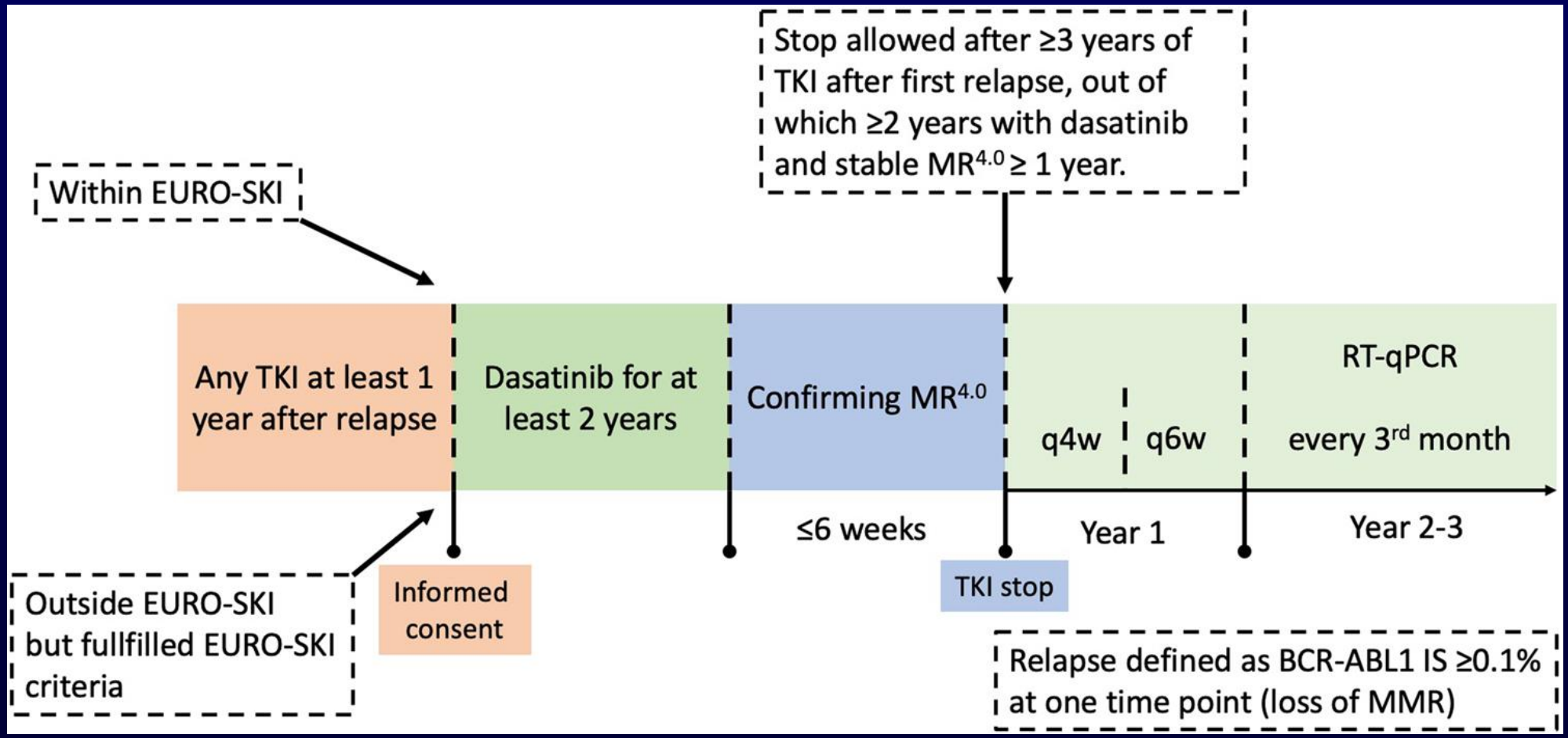


3 mo BCR::ABL1

1 mo BCR::ABL1

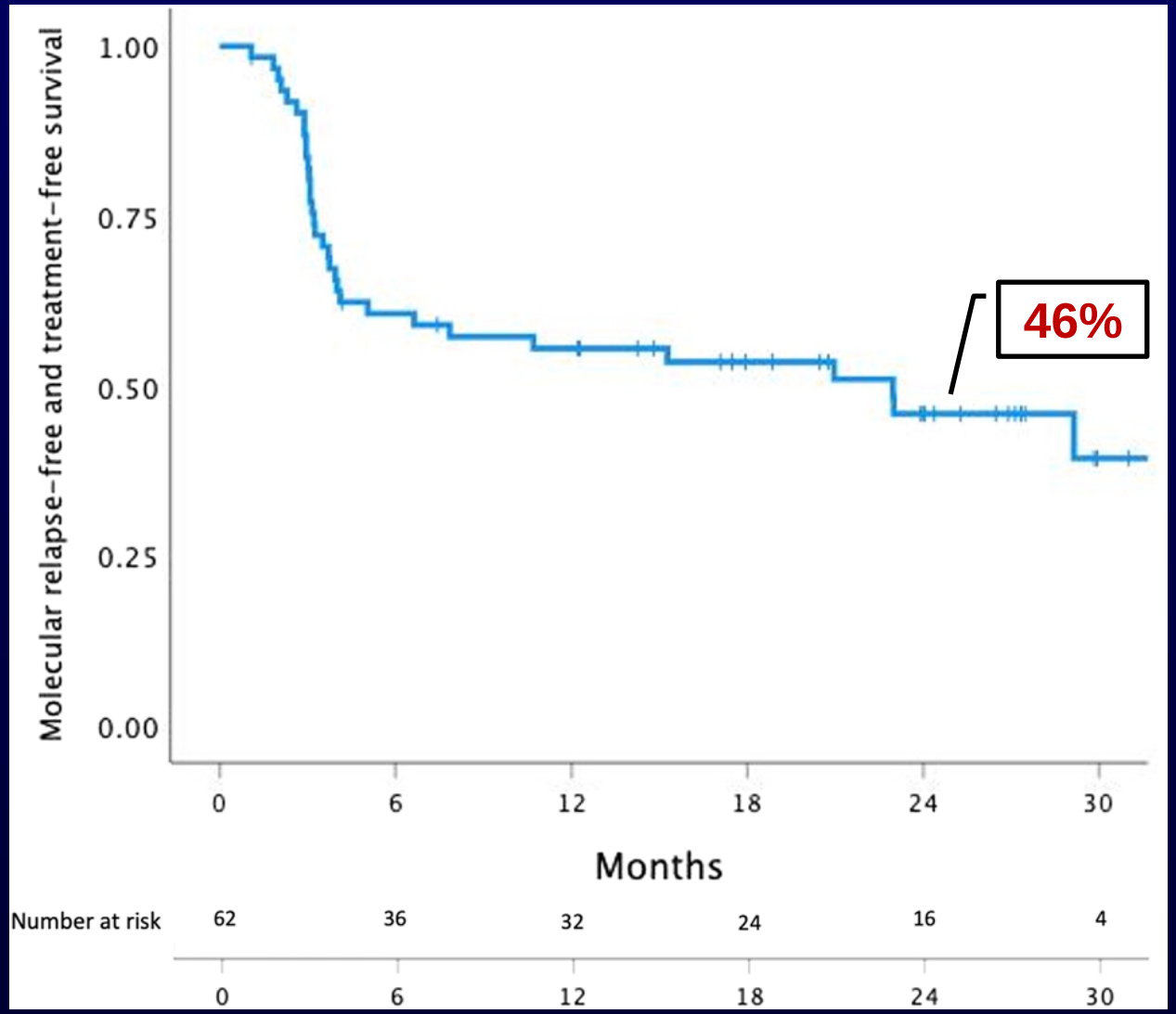
Ureshino et al. Hematol Oncol 2021; 39: 549-57

DAstop2 Trial



Flygt et al. Leukemia 2024; 38: 781-7

DAstop2: TFR after 2nd TKI discontinuation

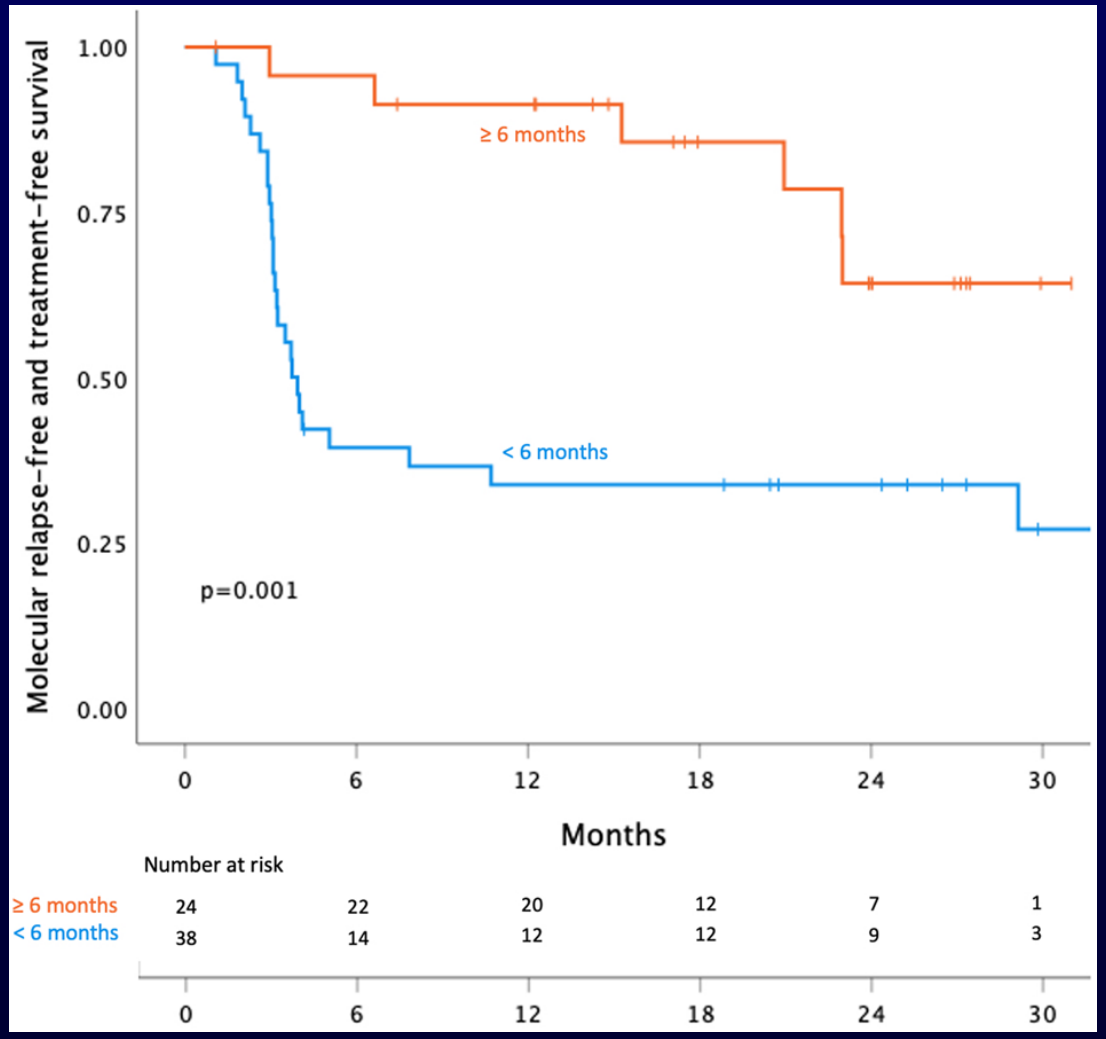


Failure rate by TKI prior to 1st attempt:

- **Imatinib: 42% failure**
- **Dasatinib: 67% failure**

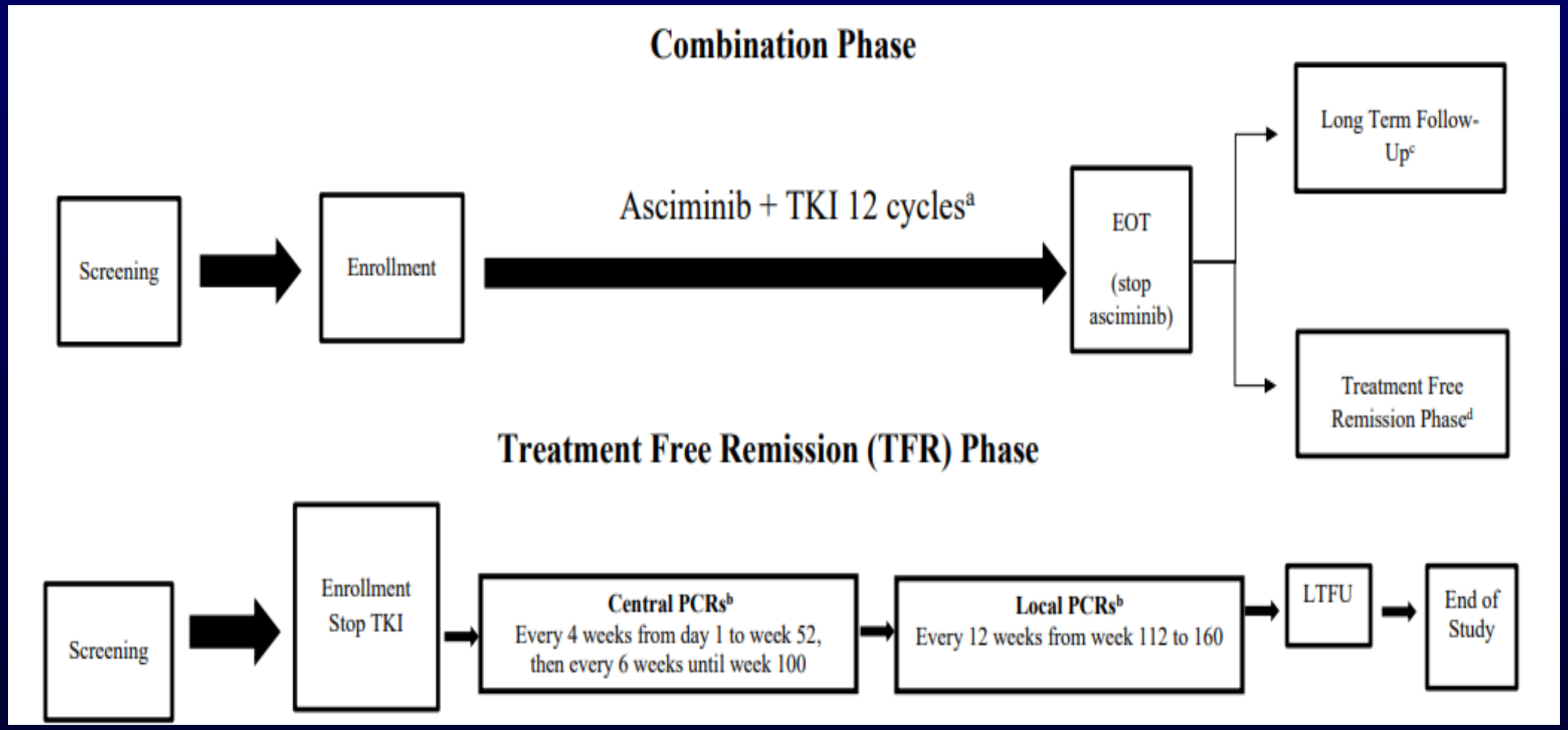
Flygt et al. Leukemia 2024; 38: 781-7

DAstop2: TFR after 2nd TKI Discontinuation by 1st TFR Duration

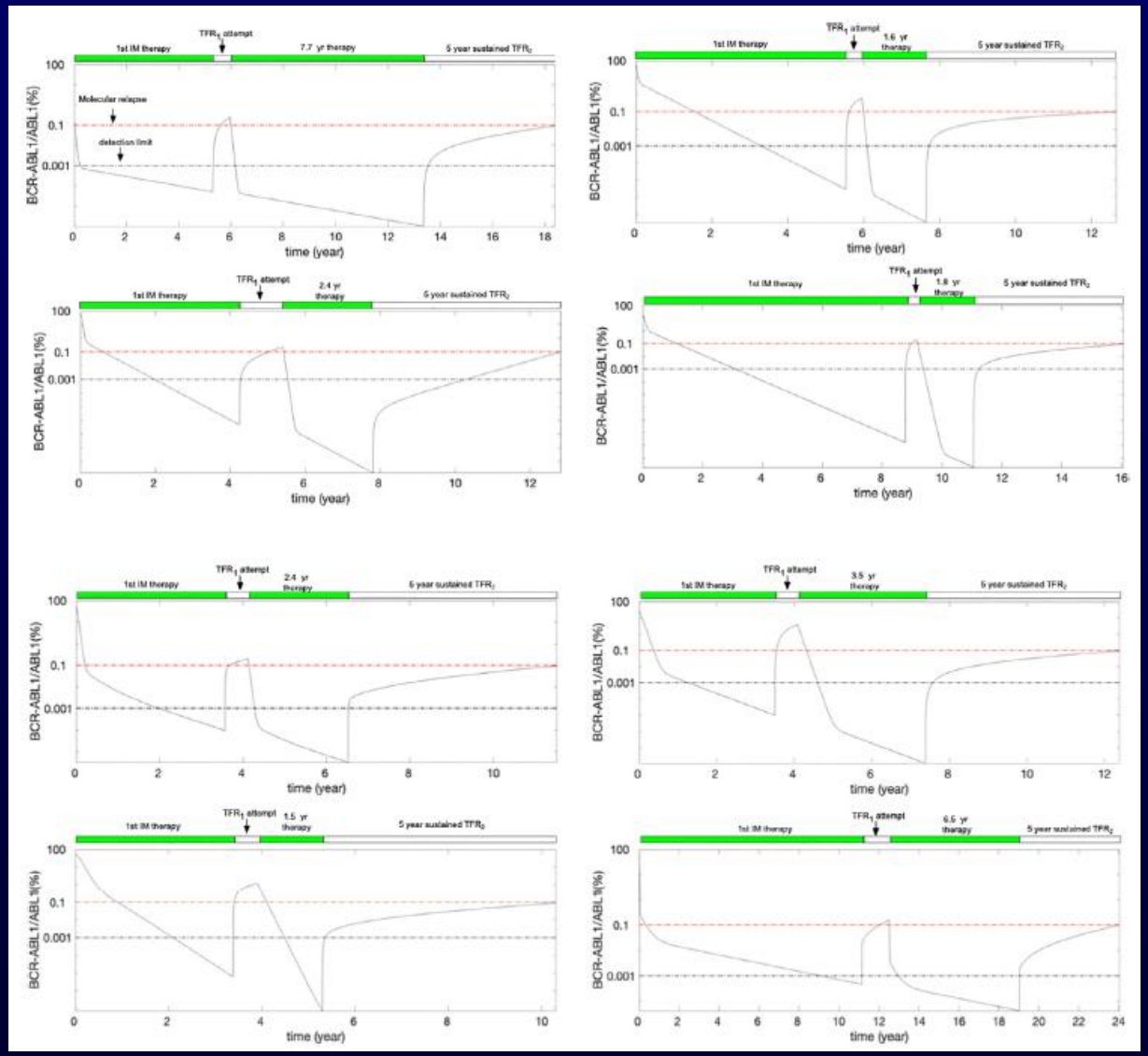


Flygt et al. Leukemia 2024; 38: 781-7

Asciminib for 2nd TFR Attempt



Predicting Optimal Duration of Therapy Before 2nd TFR



Kim et al. Neoplasia 2022; 32: 100817

Second TFR Attempt – My Take

- Is it feasible: Yes
- Is it successful: Yes (somewhat less)
- Predictors: BCR::ABL1 kinetics after 1st TFR
- What may help:
  - Deeper DMR
  - Longer duration of DMR
  - Longer treatment
  - Maybe not: different TKI
  - TBD: combinations

“Success and happiness spring from facing failure after failure with enthusiasm” Winston Churchill

“But with caution and realism: be realistic but optimistic” JC

Questions?

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