POST-NEW ORLEANS 2022
Novità dal Meeting della Società Americana di Ematologia

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Milano
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COORDINATORI
Angelo Michele Carella
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BOARD SCIENTIFICO
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SESSIONE - SINDROMI MIELOPROLIFERATIVE

Leucemia mieloide cronica

DICHIARAZIONE

Massimo Breccia

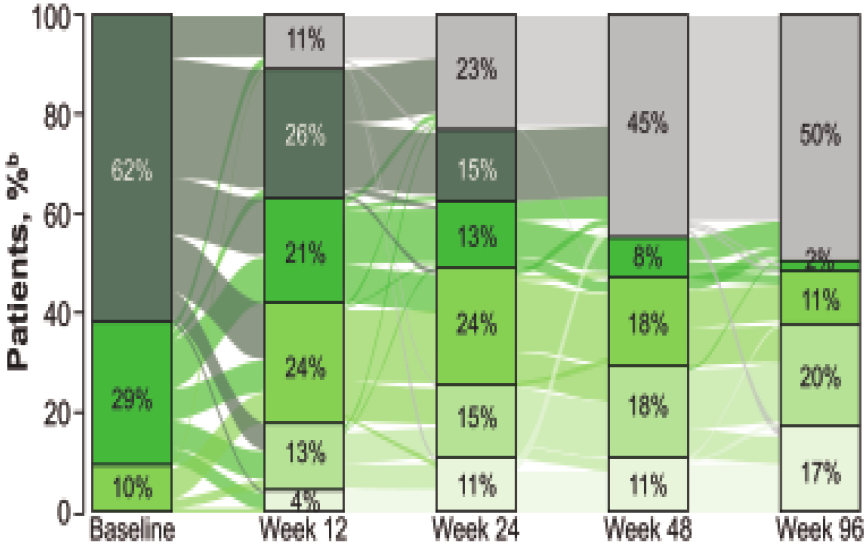
Come da nuova regolamentazione della Commissione Nazionale per la Formazione Continua del Ministero della Salute, è richiesta la trasparenza delle fonti di finanziamento e dei rapporti con soggetti portatori di interessi commerciali in campo sanitario.

- Posizione di dipendente in aziende con interessi commerciali in campo sanitario **(NIENTE DA DICHIARARE)**
- Consulenza ad aziende con interessi commerciali in campo sanitario **(Novartis, BMS, Incyte, Pfizer, Abbvie)**
- Fondi per la ricerca da aziende con interessi commerciali in campo sanitario **(NIENTE DA DICHIARARE)**
- Partecipazione ad Advisory Board **(Novartis, BMS, Incyte, Pfizer, Abbvie)**
- Titolarietà di brevetti in compartecipazione ad aziende con interessi commerciali in campo sanitario **(NIENTE DA DICHIARARE)**
- Partecipazioni azionarie in aziende con interessi commerciali in campo sanitario **(NIENTE DA DICHIARARE)**
- Altro

New TKIs

ASCEMBL trial: dynamic of responses

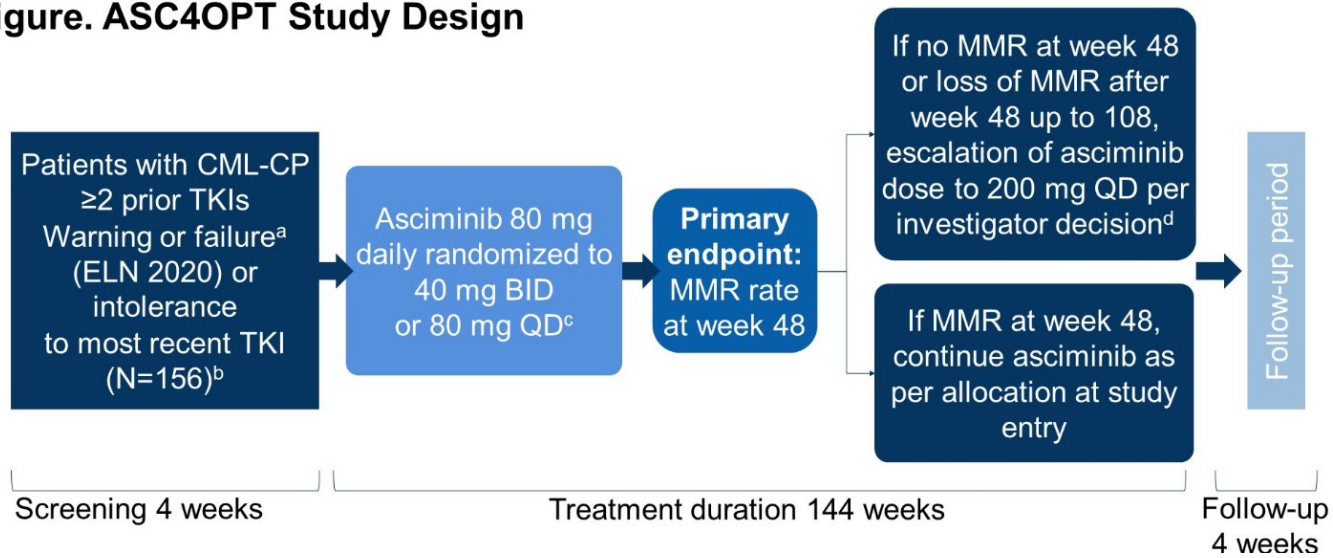
- Of 60 pts on asciminib with ***BCR::ABL1*^{IS} ≤10%** at baseline, 18 (30.0%), 24 (40.0%), and 36 (60.0%) reached MMR at wk 12, 24, and 96, respectively,
- Of 97 pts with ***BCR::ABL1*^{IS} >10% at baseline**, 10 (10.3%), 16 (16.5%), and 23 (23.7%) reached MMR at wk 12, 24, and 96, respectively,
- Of 18 pts on asciminib with ***BCR::ABL1*^{IS} >1% by wk 24**, the estimated cumulative incidence of *BCR::ABL1*^{IS} ≤1% (95% CI) was 22.2% (6.5%-43.6%) by 1 year and 38.9% (16.4%-61.0%) by 2 years.
- **Responses continued to deepen over time with asciminib in pts with CML-CP after ≥2 prior TKIs, with additional pts achieving MMR at later time points.**



Hughes et al ASH 2022; 3008

ASC4opt: asciminib as 3L (40 mg BID vs 80 mg QD)

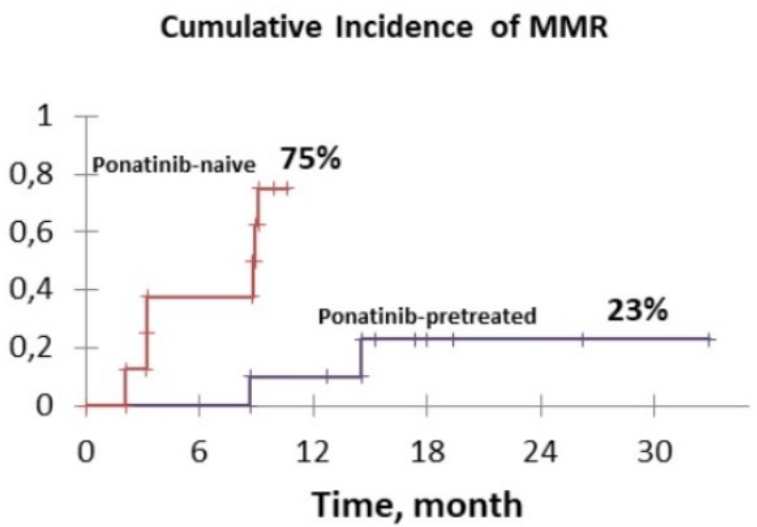
Figure. ASC4OPT Study Design



The primary endpoint is MMR rate (*BCR::ABL1*^{IS} ≤0.1%) at wk 48 in pts not in MMR at baseline. In pts not achieving MMR at 48 wks or losing response after wk 48 and up to wk 108, asciminib dose may be escalated to 200 mg QD if in the investigator's opinion the pt may benefit from the escalation.

Breccia et al ASH 2022; 4334

Asciminib MAP in Russia: updated results



- **50 patients**
- 20 pts received 200 mg BID and 30 40 mg BIS
- Median FU 17 months

- 2-year OS was 100% and 93% in 200 mg BID and 40 mg BID, respectively

For 40 mg BID group
- CCyR 55%
- **MMR 29%**
- MR4 17%

For 200 mg BID group
- CCyR 45%
- **MMR 48%**
- MR4 45%

Cumulative incidence higher in ponatinib naïve
Most frequent AEs were thrombocytopenia and neutropenia

Turkina et al ASH 2022; 4342

MAP asciminib in UK

- **53 patients**. Median age 57 years
- **62% of pts received ponatinib**
- The reason for stopping the last TKI was **intolerance in 33 (62%)** and resistance in 20 (38%) patients.
- **T315I was most common** (n=13, 25%)
- **29 (52%) achieved major molecular response (MMR**; *BCR::ABL1* PCR <0.1% IS) or better.
- History of a non-T315I-TKDM was associated with a lower rate of MMR (27% vs 62%, p=0.014).
- No significant differences were seen between those who had previously received ponatinib or not (48% vs 65%, p=0.450), although those with ponatinib resistance, rather than intolerance, had a tendency toward a lower rate of MMR (33% vs 65%, p=0.11).

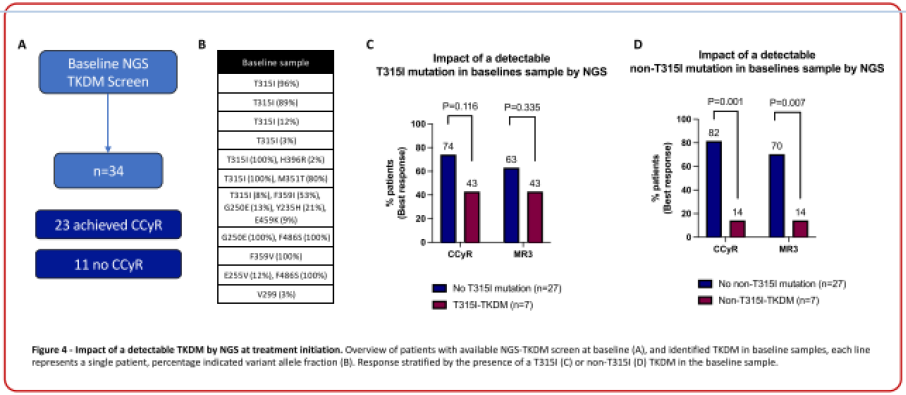
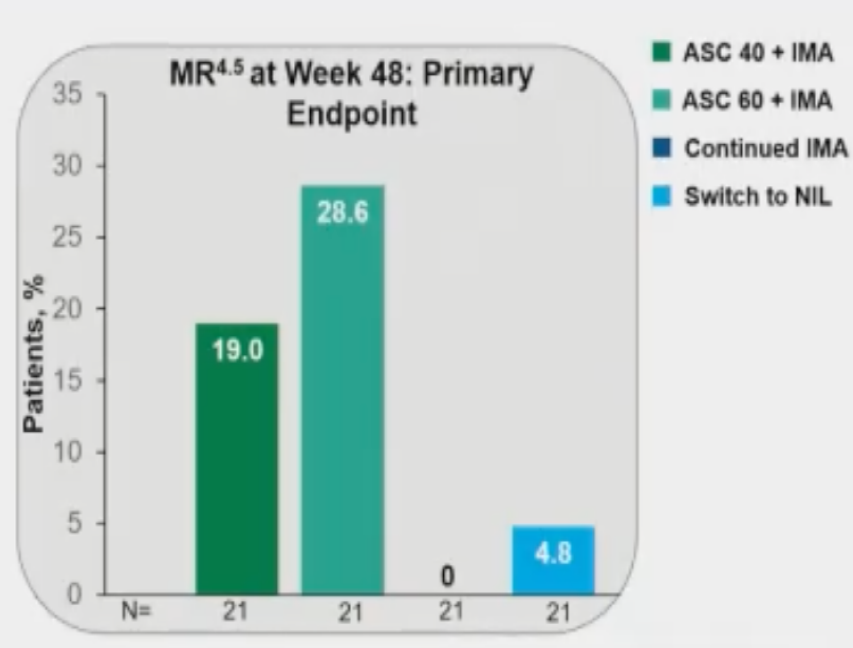


Figure 4 - Impact of a detectable TKDM by NGS at treatment initiation. Overview of patients with available NGS-TKDM screen at baseline (A), and identified TKDM in baseline samples, each line represents a single patient, percentage indicated variant allele fraction (B). Response stratified by the presence of a T315I (C) or non-T315I (D) TKDM in the baseline sample.

Innes, ASH 2022; abstract 3025

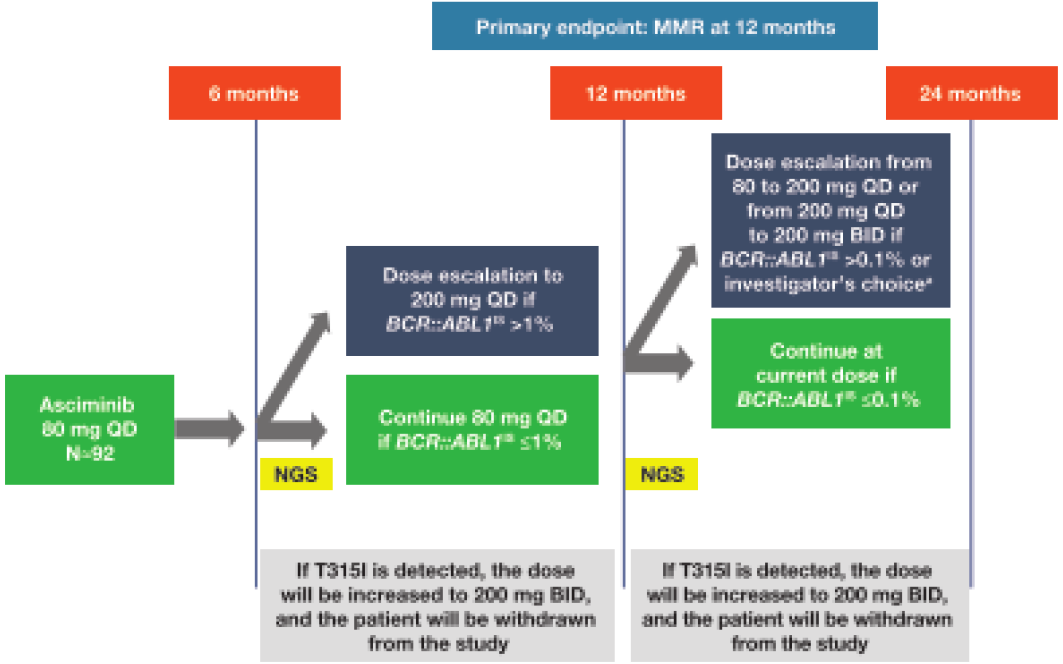
ASC4more trial: asciminib add-on vs ima vs nilo

- Pts were randomized 1:1:1:1 to receive ASC (40 or 60 mg once daily [QD]) add-on to IMA 400 mg QD, continue IMA 400 mg QD, or switch to NIL 300 mg twice daily. The primary endpoint was $MR^{4.5}$ rate at wk 48.
- **84 pts randomized**
- In the 40-mg ASC add-on, 60-mg ASC add-on, IMA, and NIL arms, respectively, 19.0%, 28.6%, 0%, and 4.8% of pts were in $MR^{4.5}$ at wk 48
- The Kaplan-Meier–estimated rate of maintaining $MR^{4.5}$ for ≥48 wk was 60.0%, 80.0%, and 66.7% in the 40- and 60-mg ASC add-on and NIL arms, respectively.
- ASC add-on was associated with higher rates of adverse events (AEs), serious AEs, and discontinuations than continued IMA, but less than switching to NIL



Cortes et al ASH 2022; 80

ASC2ESCALATE: dose escalation to 200 mg BID in pts with failure

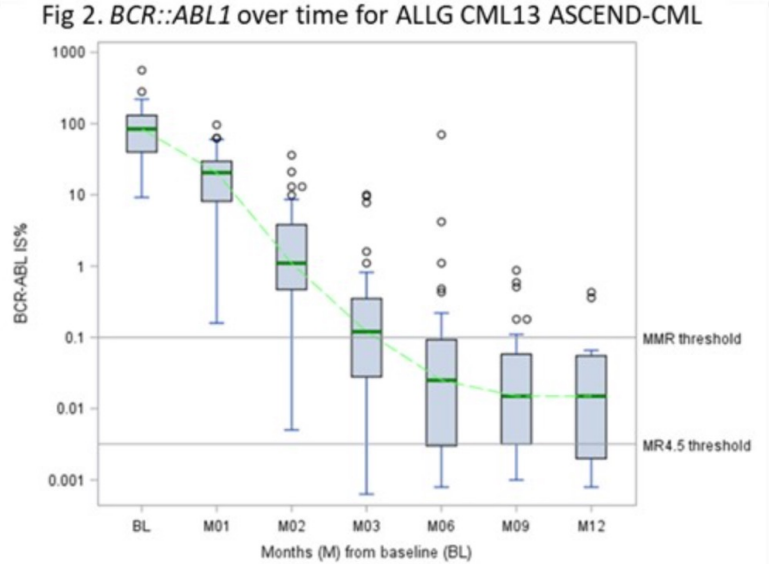


A Phase II, Single-Arm, Dose-Escalation Study of Asciminib Monotherapy in Patients With Chronic Myeloid Leukemia in Chronic Phase Previously Treated With 1 Prior TKI

Sasaki et al ASH 2022; 3020

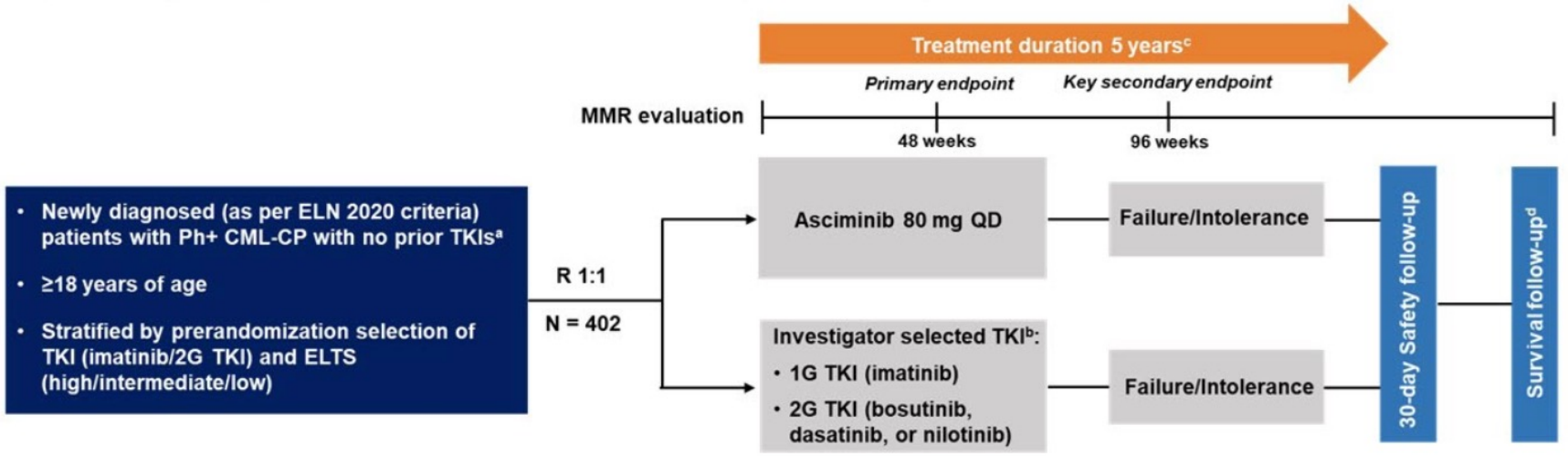
ASCEND trial: asciminib 1st line interim analysis

- Phase II trial
- Patients with treatment failure (*BCR::ABL1* >10% at 3 or 6 months; *BCR::ABL1* >1% at 12 or 18 months) continue asciminib and add either imatinib, dasatinib or nilotinib, according to physician preference.
- Patients who have not failed, but have not achieved optimal response at 6, 12, or 18 months, have their asciminib dose doubled to 80mg BID
- Co-primary end points are achievement of early molecular response (EMR, *BCR::ABL1* ≤10% at 3 months) and major molecular response (*BCR::ABL1* ≤0.1%) by 12 months
- **79/100 pts enrolled with a median FU of 10 months**
- Most common AEs reported were neutropenia, thrombocytopenia, increased amylase/lipase
- 9 pts discontinued: 2 case of resistance (1 sudden BC with myristoilic site mutations)
- **EMR 93.7%**
- 3 pts escalated the dose



Yeung et al ASH 2022; 79

ASC4first: asciminib as frontline Tx



The primary objectives are to compare the efficacy of asciminib vs investigator-selected TKIs and to compare the efficacy of asciminib vs IMA in the stratum of investigator-selected IMA. The primary endpoint is MMR at week 48. The study will be positive if either of these objectives is met.

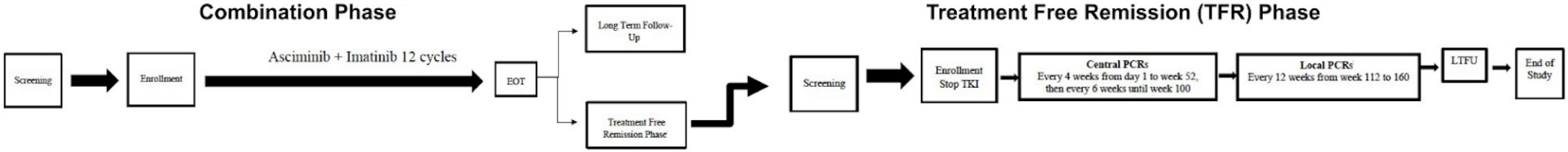
Hughes et al ASH 2022; 3012

Asciminib post TFR failure

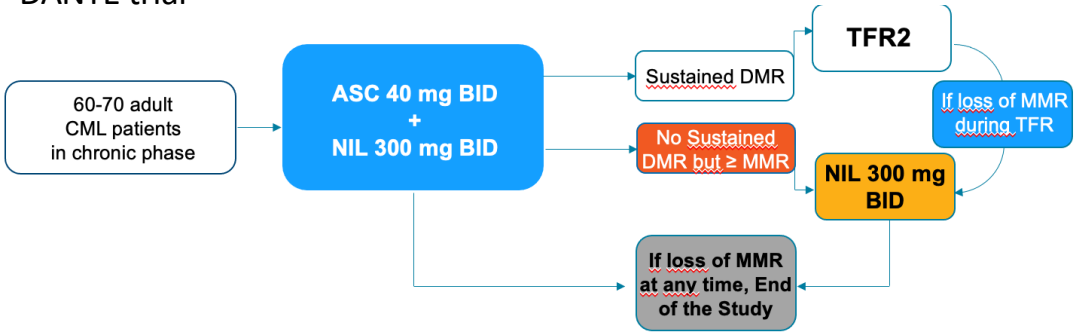
Inclusion Criteria:

1. Age ≥18 years old; ECOG PS 0-3
2. CML-CP with either the b3a2 (e14a2) or b2a2 (e13a2) variants giving rise to the p210 BCR-ABL1 protein
3. Single prior instance of physician guided TFR attempt
4. ≥ 3y of TKI therapy and documented deep MR (MR4; <0.01% IS) for ≥ 2 years prior to first TFR attempt
5. Relapse (loss of MMR) and resumption of imatinib (up to 400 mg daily) for 1 year prior to study entry
6. BCR::ABL1 RQ-PCR <0.0032% IS at enrollment
7. Willing to practice appropriate contraception

Khoury-center



DANTE trial



Inclusion criteria

- CML-CP patients ≥ 18 years
- First line treatment with NIL for at least 3 calendar years at 300 mg BID dose (it may be less than 300 mg BID if considered appropriate by clinical judgement, but at least 300 mg daily), followed by first TFR attempt
- First TFR failure, followed by at least 1 year of NIL retreatment before enrollment in TFR2 stage
- MR4 or better (BCR-ABL ≤ 0.01% IS) assessed at screening

Mauro et al ASH 2022, abstract
Rosti et al ASH 2022, abstract

Olverembatinib: phase 1, 5-years long-term FU

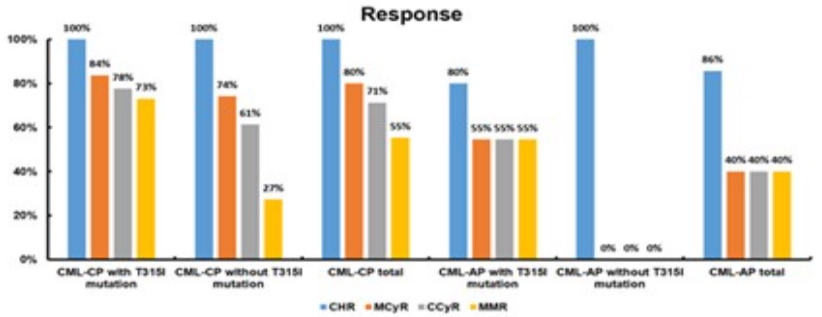
- Phase I trial, 101 pts (86 CP)
- Median Tx duration 44.7 months
- 83% >2 previous TKIs
- 66.7% T315I mutated, 11.9% compound mutations
- 71% continued the treatment

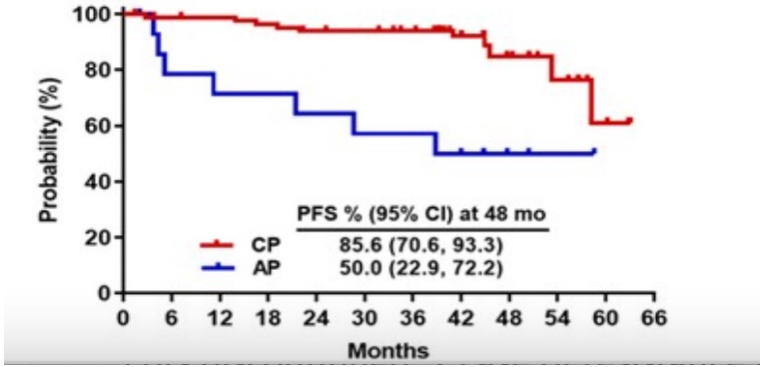
- CP patients: **55% MMR**
- AP patients: 40% MMR

- **T315I mutated: 73% MMR**

- PFS at 48 mos: 85.6%
- 7/12 compound obtained MMR (58%)

- AE: skin pigmentation 85%
  hypertriglyceridemia 11%
  proteinuria 6.9%
  thrombocytopenia 78% (51% > GR3)





Jiang et al ASH 2022; 81

Olverembatinib in T315I mutated pts: phase 2 trial

- **CC201 study (CP with T315I, 40 mg QD)**

41 pts

78% pretreated with > 2 TKIs

100% CHR, 82.9% MCyR, **58.5% MMR**

36-months PFS 86.3%, OS 95%

AEs: thrombocytopenia 70.7%, skin pigmentation 56.1%

- **CC202 study (AP pts with T315I)**

23 pts,

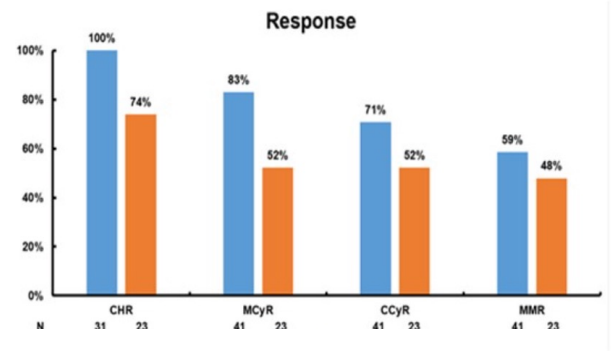
78.3% MaHR (73.9% CHR), 52% MCyR, **47.8% MMR**

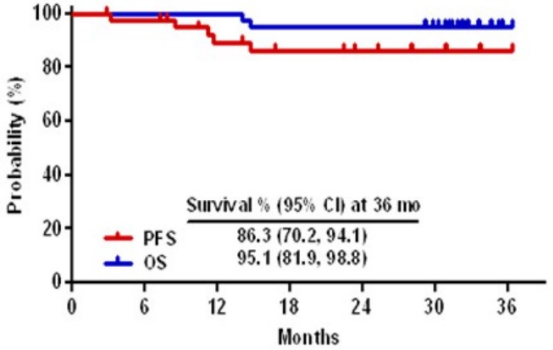
36-months PFS 57%, OS 69.6%

AEs: thrombocytopenia 78.3%, skin pigmentation 69.6%

56% proteinuria and 52% hypocalcemia

61% hypertriglyceridemia





Jiang et al ASH 2022; 83

Olverembatinib phase 2 MDACC trial

- 30 pts
- Randomized 3:3:2 to olverembatinib 30, 40, 50 QOD
- The majority (56.7%) received 4 or 5 previous TKIs
- 21 received ponatinib and 5 asciminib before
- 12 T315I mutated

- 22/30 pts experienced GR 3/4 AEs
- Thrombocytopenia 23%
  neutropenia 16%
  CPK increased 10%

- In CP: CCyR 66.7%, MMR 44%

- The drug was effective in T315I mutated or WT, regardless the previous treatment with ponatinib or asciminib

Table 2. Efficacy Overview of Olverembatinib in Patients with CML and Ph+ ALL

Response Category	Total	CML-CP	CML-AP/BP/Ph+ ALL	Pts With T315I Mutation	Pts Without T315I Mutation
Efficacy population	21	16	5	8	13
Cytogenetic response					
Evaluable subjects, no.	17	13	4	8	9
Major cytogenetic response, no. (%)	11 (64.7)	9 (69.2)	2 (50.0)	5 (62.5)	6 (66.7)
Complete cytogenetic response,-no. (%)	10 (58.8)	9 (69.2)	1 (25.0)	5 (62.5)	5 (55.6)
Molecular response					
Evaluable subjects, no. (%)	21	16	5	8	13
Major molecular response, no. (%)	9 (42.9)	7 (43.8)	2 (40.0)	4 (50.0)	5 (38.5)

Response Category		Ponatinib-Pretreated	Ponatinib-Naïve	Ponatinib-Resistant	Ponatinib-Intolerant
Efficacy population		14	8	11	3
Cytogenetic response					
Evaluable subjects, no.		12	6	9	3
Major cytogenetic response, no. (%)		9 (75.0)	3 (50.0)	6 (66.7)	3 (100.0)
Complete cytogenetic response, no. (%)		8 (66.7)	3 (50.0)	5 (55.6)	3 (100.0)
Molecular response					
Evaluable subjects, no.		14	8	11	3
Major molecular response, no. (%)		7 (50.0)	3 (37.5)	6 (54.5)	1 (33.3)

Jabbour et al ASH 2022; 82

Vodobatinib efficacy according to lines of previous TKIs

- 43 pts
- 15 pts in 2L, 28 in 3L, 15 3L including ponatinib, and 3 pts in 3L including pona and asciminib

- 56% resistant, 15 with mutations
- MMR was achieved in 5 (33.3%), 14 (50.0%) and 8 (53.3%) in 2T, 3T and PON, respectively.
- Of the 20 pts with MMR as best response, 10 (23.6%) achieved molecular response M4

- Dose intensity was similar for all groups
- 2/16 who progressed, developed compound mutations

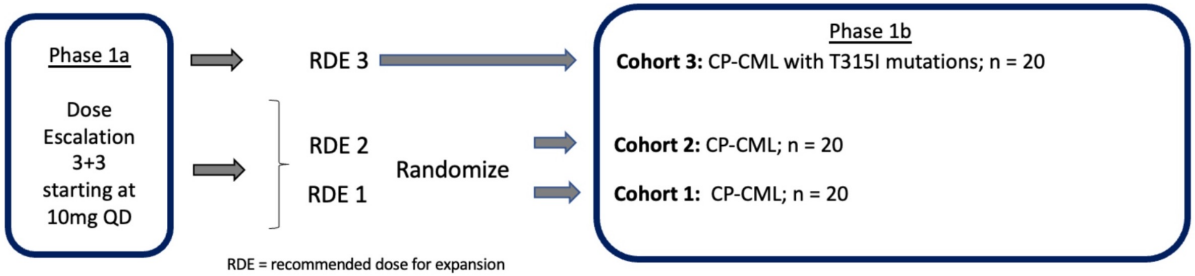
- AEs: thrombocytopenia 14%
  GI events
  increased amylase/lipase
- 10 pts experienced CV effects (GR3 in 2 pts)

Table 1: Efficacy Outcomes and Drug Exposure

Status	2T (N = 15)		3T (N = 28)		PON (N = 15)		ASC (N = 3)		Overall (N = 43)	
Hematological	**Baseline**	**Best Response**	**Baseline**	**Best Response**	**Baseline**	**Best Response**	**Baseline**	**Best Response**	**Baseline**	**Best Response**
CHR	1 (6.7)	7 (46.7)	14 (50.0)	21 (75.0)	9 (60.0)	12 (80.0)	2 (66.7)	3 (100.0)	15 (34.9)	28 (65.1)
Missing[1]	5 (33.3)	0	2 (7.1)	0	1 (6.7)	0	1 (33.3)	0	7 (16.3)	0
Cytogenetic	**Baseline**	**Best Response**	**Baseline**	**Best Response**	**Baseline**	**Best Response**	**Baseline**	**Best Response**	**Baseline**	**Best Response**
Major cytogenetic response	4 (26.7)	11 (73.3)	8 (28.6)	17 (60.7)	5 (33.3)	10 (66.7)	0	1 (33.3)	12 (27.9)	28 (65.1)
Complete cytogenetic response	2 (13.3)	10 (66.7)	5 (17.9)	14 (50.0)[2]	4 (26.7)	7 (46.7)[2]	0	1 (33.3)	7 (16.3)	24 (55.8)
Partial cytogenetic response	2 (13.3)	1 (6.7)	3 (10.7)	3 (10.7)	1 (6.7)	3 (20.0)	0	0	5 (11.6)	4 (9.3)
Minor response	1 (6.7)	0	6 (21.4)	1 (3.6)	3 (20.0)	1 (6.7)	2 (66.7)	1 (33.3)	7 (16.3)	1 (2.3)
Minimal response	2 (13.3)	3 (20.0)	5 (17.9)	4 (14.3)	1 (6.7)	1 (6.7)	0	0	7 (16.3)	7 (16.3)
No response	8 (53.3)	1 (6.7)	7 (25.0)	4 (14.3)	4 (26.7)	2 (13.3)	0	1 (33.3)	15 (34.9)	5 (11.6)
Missing	0	0	2 (7.1)	2 (7.1)	2 (13.3)	1 (6.7)	1(33.3)	0	2 (4.7)	2 (4.7)
Molecular	**Baseline**	**Best Response**	**Baseline**	**Best Response**	**Baseline**	**Best Response**	**Baseline**	**Best Response**	**Baseline**	**Best Response**
Major molecular response (M3)	0	5 (33.3)	1 (3.6)	15 (53.6)	0	8 (53.3)	0	0	1 (2.3)	20 (46.5)
Molecular Response (M4)	0	2 (13.3)	1 (3.6)	9 (32.1)	0	4 (26.7)	0	0	1 (2.3)	11 (25.6)
No response	14 (93.3)	10 (66.7)	24 (85.7)	12 (42.9)	13 (86.7)	7 (46.7)	1 (33.3)	3 (100.0)	38 (88.4)	22 (51.2)
Missing	1 (6.7)	0	3 (10.7)	1 (3.6)	2 (13.3)	0	2 (66.7)	0	4 (9.3)	1 (2.3)
Average dose received per day across all cycles (median, range in mg)	**174.00 (58.7 – 204.0)**		**127.7 (48.0 – 215.1)**		**123.7 (66 -0 – 215.1)**		**123.7 (66.0 – 167.7)**		**166.6 (48.0 – 215.1)**	

Cortes et al ASH 2022; 84

ELVN-001: new selective TK inhibitor



- ELVN-001 is a highly selective small molecule active site inhibitor of ABL1 that does not significantly inhibit the receptor tyrosine kinases PDGFR, KIT, VEGFR2 or the Src-family (eg SRC, LCK, LYN, FYN).
- In vitro data also supports ELVN-001 targeting the most common CML mutation, T315I and not being a substrate for drug efflux transporters such as BCRP, which may contribute to resistance or sensitivity to other TKIs.
- A phase 1 open-label, multi-center, dose escalation and expansion study. Eligible pts are adults with CP and AP CML who are intolerant or have failed (as per ELN 2020 Recommendations) available TKIs known to be active for treatment of their CML.
- Prior marrow transplant is allowed. CML with point mutations E255, Y253, G250, F317 or Q252 are excluded.
- Primary endpoints are dose limiting toxicities, adverse events, laboratory and ECG abnormalities.

Hughes et al ASH 2022; 3018

Update of ongoing trials

OPTIC trial at 3 years of FU

- 283 pts randomized to 3 different doses
- Of the patients with T315I mutations, 64% (16/25), 25% (5/20), and 16% (3/19) attained ≤1% *BCR::ABL1*^{IS} by 36 months versus 59% (39/66), 44% (32/73), and 46% (33/71) of patients without T315I in the 45-mg, 30-mg, and 15-mg cohorts, respectively.
- 27% (12/45) and 11% (3/27) patients re-escalated after loss of ≤1% *BCR::ABL1*^{IS} response; 75% (9/12) and 67% (2/3) of these patients regained ≤1% *BCR::ABL1*^{IS}, respectively.
- Grade ≥3 AOEs were reported in the 45-mg cohort (6%), 30-mg cohort (6%), and 15-mg cohort (4%) and were similar to reported rates in the primary analysis of OPTIC (45 mg, 5%; 30 mg, 5%; 15 mg, 3%).

Response[a]	45-mg Cohort (N=93)	30-mg Cohort (N=93)	15-mg Cohort (N=91)
≤1% *BCR::ABL1*^{IS} by 36 mo, n (%)	56 (60)	37 (40)	36 (40)
Median DOR, mo (range)	NR (0–68.8)	NR (0–66.1)	NR (0–69.5)
Survival probability at 36 mo, % (95% CI)			
PFS	72 (61–81)	67 (54–77)	70 (57–79)
OS	87 (78–93)	87 (78–93)	92 (85–96)

Cortes et al ASH 2022; 620

Dasatinib 50 mg frontline long-term FU

- 83 pts
- Median age 47 years
- 48% were males

- 65% of pts had low risk

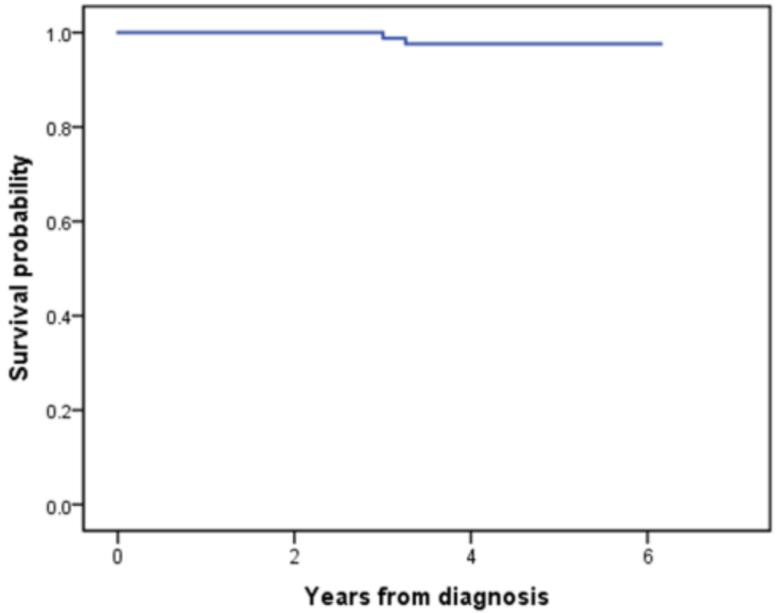
- At 3 months, 96% achieved EMR

- At 12 months, 81% MMR, 63% MR4, 46% MR4.5

- 5-years FFS 88%, EFS 97%, OS 98%

- Rate of PE was 5%

- 5 patients discontinued the treatment



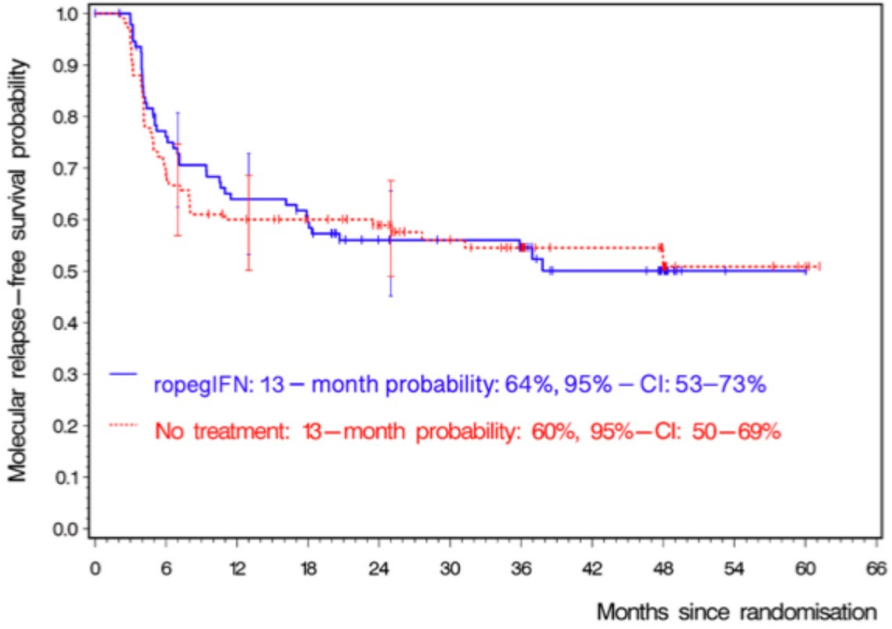
Ricos et al ASH 2022; 619

TFR

Emerging strategies: the role of ropeg-IFN in TFR

- Pts in stable DMR or in second TFR randomized to receive ropeg-IFN or no other treatment
- Primary endpoint the molecular relapse free survival
- 203 pts randomized
- In 80% of pts was the first attempt of TFR
- MRFS at 24 months was 56% for ropeg-IFN vs 59% for no treatment arm

- Ropeg-IFN maintenance after discontinuing TKI-monotherapy **does not increase** the proportion of patients, who persistently maintain at least an MMR. The German CML-V (TIGER) trial currently explores the impact of IFN maintenance on TFR when patients receive a combination of TKI plus IFN before TKI stop



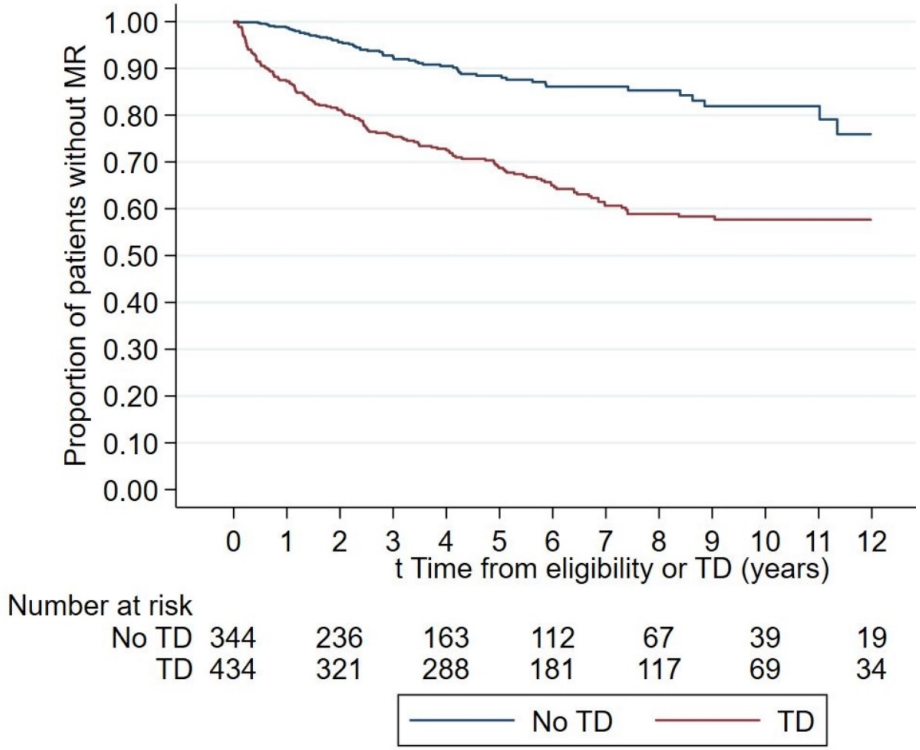
Burchert et al ASH 2022; 622

TFR-pro: risk of progression in pts eligible to TFR

- Retrospective study in 20 centers
- Pts eligible have at least 4 years of TKI treatment and 18 months of stable DMR
- Primary endpoint was to assess the risk of progression to AP/BP
- 810 pts recorded
- Median FU 6 years

- 434 pts attempted TFR, with 35% of relapse
- Risk of progression is 1/778 (0.13%)

- Slightly more than half of 778 eligible Pts attempt TD
- Pts who discontinue treatment have a significantly higher risk of losing MR3 than Pts who do not



Zambrotta et al ASH 2022; 6239

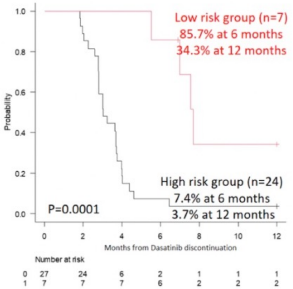
TRAD trial: second attempt TFR

- Dasatinib for rechallenge after 1st TFR failure with imatinib
- 12 months dasatinib did not improve TFR2 rate
- 3/35 pts that stopped dasatinib maintained TFR (8.6%)
- MRFS at 12 months was 10%
- Clinical factors predictive of TFR2 failure were: 1. failure to achieve MMR in less than 1 month following dasatinib rechallenge; 2. doubling time below 12.7 days at 2 months after imatinib discontinuation; 3. any detectable BCR::ABL1 transcript level between MR4 and MR4.5 before dasatinib discontinuation.
- A model was created with these 3 variables predictive of TFR2 failure

Table 1. Univariate analysis of TFR2 risk factors identified 5 risk factors

Risk factor	Subgroup	TFR2, 6 mo	P-value	HR [95% CI]
During DA rechallenge				
Time to MMR with DA	MMR achieved beyond 1 mo (n=24)	63.6%	0.0002	1.000
	MMR achieved within 1 mo (n=11)	4.2%		4.656 [1.945-11.14]
Prior to DA discontinuation for TFR2				
BCR::ABL1 qPCR level before TFR2	Undetectable (MR5.5 or below) (n=28)	28.6%	0.0001	1.000
	Any detectable (MR4-MR5.4) (n=6)	0%		7.04 [25.6-1.964]
IM discontinuation for TFR1				
Molecular relapse pattern	MR4 loss only (n=11)	63.6%	0.001	1.000
	MMR loss (n=24)	4.2%		4.163 [1.749-9.901]
Time to MR loss	MR loss beyond 2.8 mo (n=21)	38.1%	0.0002	1.000
	MR loss within 2.8 mo (n=14)	0%		4.717 [2.058 -10.81]
DT at 2 months	DT above 12.75 days or ≤ 0 (n=12)	50.0%	0.002	1.000
	shorter DT at 2 months (n=22)	4.5%		3.654 [1.59-8.396]

Fig 1. TFR2 according to the risk group of risk score model



Perusini et al ASH 2022; 3017

DANTE: dose optimization trial for TFR

Primary endpoint: Percentage of patients in FTFR 96 weeks after the start of consolidation phase

FTFR: Patients in MMR or better including those who remained in discontinuation during TFR phase and those who are treated with half the standard dose at week 96

Screening Week 4-0 → **Consolidation Phase Week 0-48**

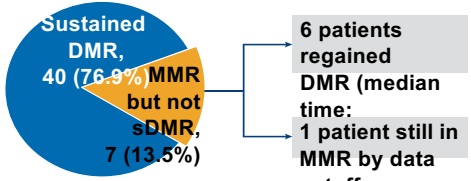
- CML-CP ≥18 years
- Nilotinib first line for at least 3 calendar years at 300 mg BID dose. At study entry, an ongoing treatment at a dose ≥ 400 mg per day is allowed.
- Sustained DMR, defined as MR 4.0 in all of the last 4 BCR-ABL RQ-PCR assessments
- No prior TFR attempt or known atypical transcript
- ECOG performance status 0-2

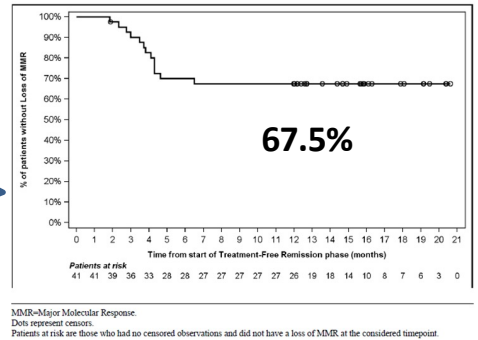
FTFR: patients in MMR or better at week 96

- Sustained DMR → TFR Week 48-144
- No sustained DMR but ≥ MMR → Remain in consolidation until Week 144
- Loss of MMR → Return to standard treatment until

Patients with loss of MMR at any time will return to standard nilotinib regimen (300 mg BID) until end of trial (week 144).

Molecular response in 47 patients who completed Consolidation Phase





Stagno et al, ASH 2022, 4326

Genomic data

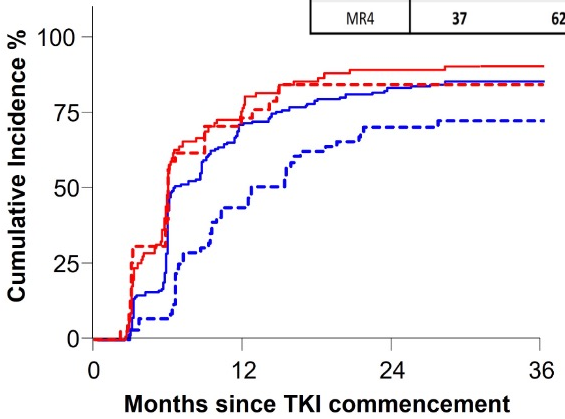
Additional mutation events in CML: prognostic role

- True incidence of effect of cancer-gene mutations and Ph-associated rearrangements
- Incidence of AME in imatinib-treated pts was 31% (16% gene mutations and 18% Ph-rearrangements)
- Incidence of AME in 2gen TKIs-treated pts was 29% (17% gene mutations and 14% Ph-rearrangements)
- ASXL1 was the most frequent mutation (9% and 8%)

- **Imatinib-treated pts with AME had low FFS (69%), MMR (72%) and MR4 /37%)**
- In 2gen TKIs pts similar responses in pts with AME

- No differences in OS and TFS in imatinib and 2gen TKIs

Outcome by 36 months	Imatinib-treated patients (n=200)			2G-TKI treated patients (n=116)		
	Patients with AMEs (%); n=61	Patients without AMEs (%); n=139	P value	Patients with AMEs (%); n=34	Patients without AMEs (%); n=84	P value
Failure-free survival	**69**	**84**	**.03**	91	94	.47
Major molecular response	**72**	**84**	**.02**	83	88	.71
MR4	**37**	**62**	**.001**	63	70	.40



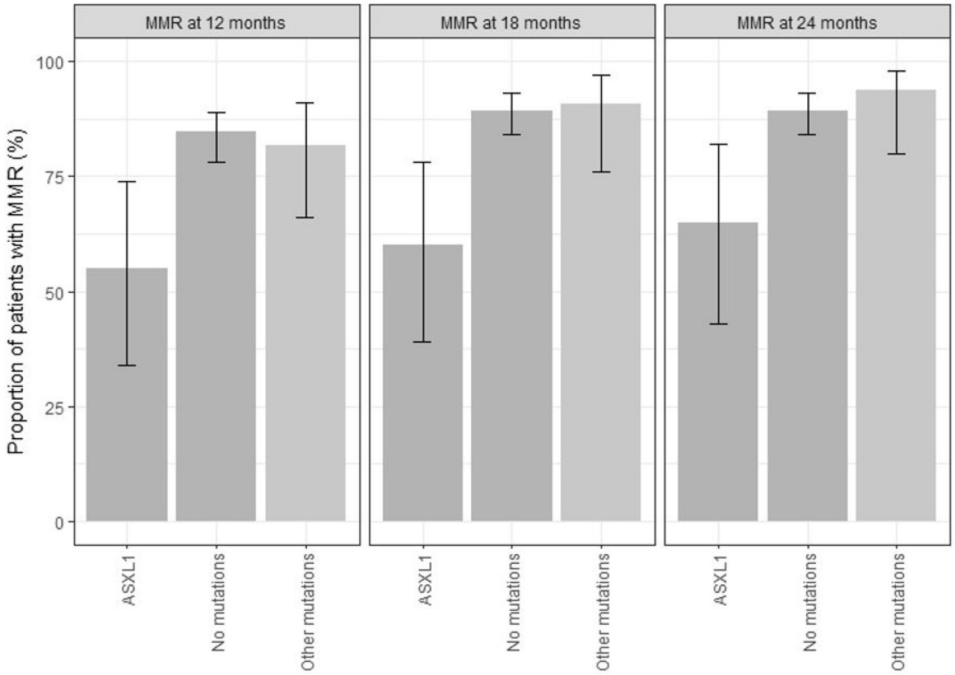
Shanmuganathan et al ASH 2022; 331

ASXL1 in CML: prognostic role

- 222 pts of TIGER study investigated at baseline with NGS
- 53 pts (24%) carried 60 gene mutations
- ASXL1 in 20 pts (9%)
- Median age 54 years

- Follow-up of 100 pts during Tx showed 3 distinct patterns
- Eradication in parallel with BCR::ABL1
- Persistence despite decline of BCR::ABL1
- Emergence or clonal evolution

- **Pts with ASXL1 showed less favourable response to nilotinib for MMR (at 24 months 65% vs 89%)**
- ASXL1 mutated were more frequently found in high risk EUTOS score and were more younger



Ernst et al ASH 2022; 332