Actualités thérapeutiques dans la LMC: Asciminib

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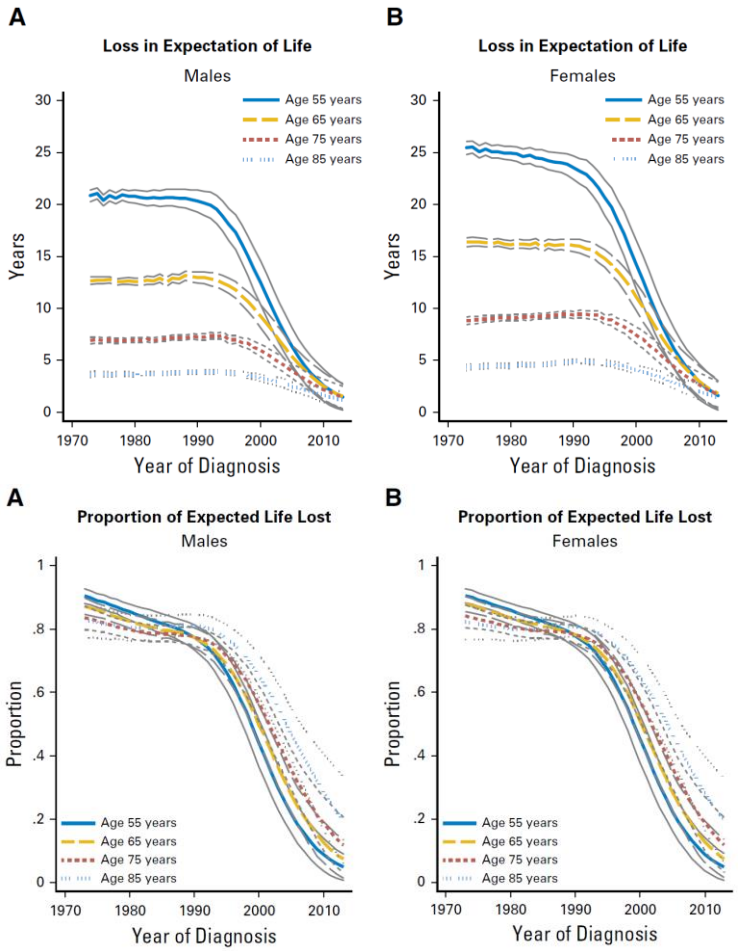
04/04/2023

Rappel très court LMC en 2023

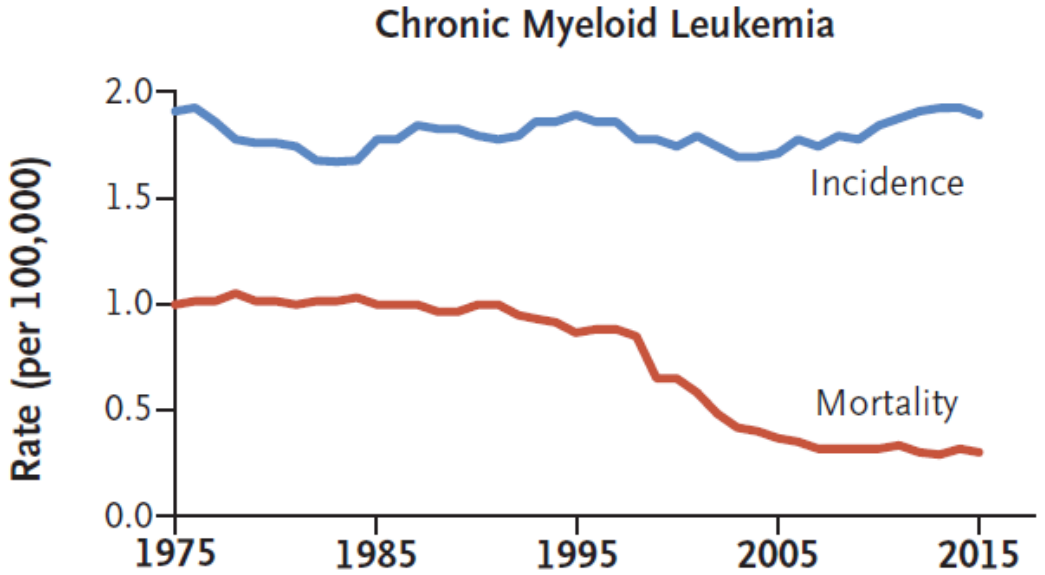
LMC: nouvelle espérance de vie

- La perte d'espérance de vie a diminuée très significativement avec les décennies



Bower, JCO 2016

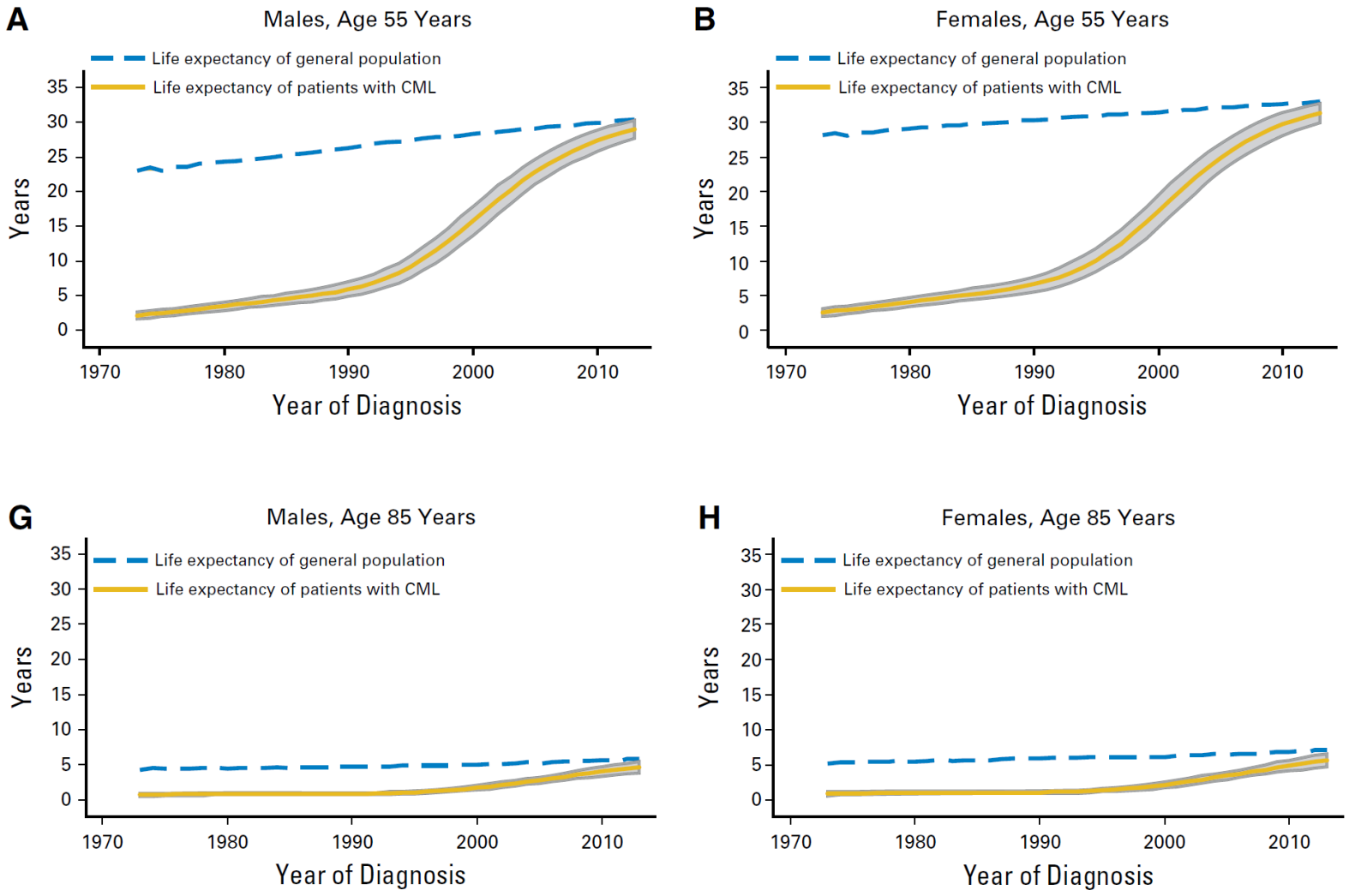
Toutes les catégories d'âge Profitent de l'amélioration de la survie



Welch NEJM 2019

LMC espérance de vie

Registre suédois
de 1973 à 2013
N = 2 662



Toutes les catégories d'âge
profitent de l'amélioration de la survie
quasi-équivalente à la population générale

Bower, JCO 2016

LMC augmentation de la prévalence

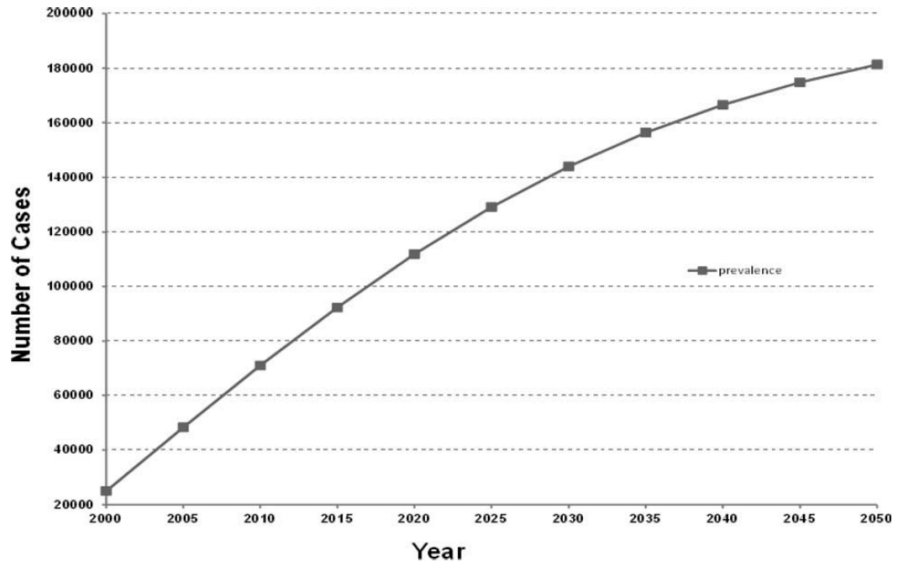
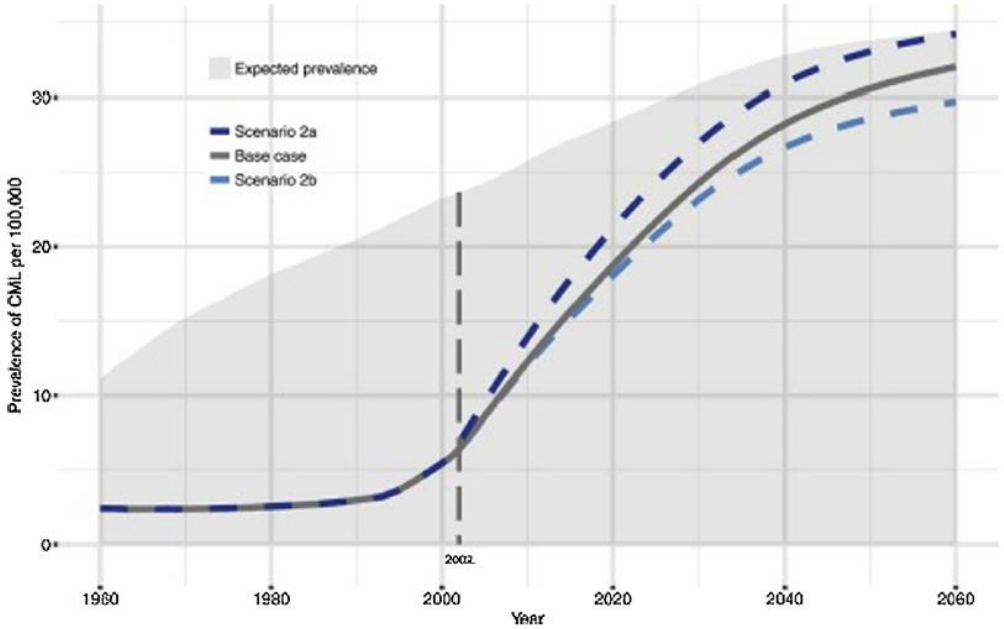


Figure 1. The estimated prevalence of chronic myeloid leukemia in the United States by calendar year is illustrated.

Huang Cancer 2012



Delord Leuk Research 2018

Prévalence x10 entre 2012 et 2040

Avec impact financier +++

Malgré les thérapies ciblées, de nombreux « BESOINS MÉDICAUX NON COUVERTS » persistent en 3ème ligne

SURVENUE DE RÉSISTANCES
après plusieurs lignes de traitement, résultant de **l'instabilité génétique** propre à la LMC (10)

INTOLÉRANCE FRÉQUENTE
suite à une exposition prolongée aux ITKs lors d'un traitement au long cours (11

ÉCHEC DU TRAITEMENT PAR ITKs (2)

ABSENCE D'OBSERVANCE (2)
30 % des patients ne seraient pas observants aux ITKs, augmentant le risque de réponse sub-optimale, de progression de la maladie et de mortalité

INTERACTIONS MEDICAMENTEUSES
avec d'autres ITKs ou un traitement concomitant (2)

Nette diminution de la survie au fur et à mesure des lignes de traitement

La diminution de la survie globale est associée

A une phase avancée de la maladie	A une réponse insuffisante en 1ère ligne de traitement	A l'interruption de la 1ère ligne de traitement pour toute autre raison

Toujours des besoins non couverts

→ Chez un patient résistant à un ITK2G, on peut faire la tentative d'un autre ITK2G. Les autres possibilités sont d'envisager un ITK3G et pour les patients éligibles une allogreffe de CSH.

→ Chez un patient sans aucune solution (autre ITK, essai clinique, allogreffe), l'objectif du traitement sera uniquement le contrôle des symptomes

LMC: est-ce que tout est réglé en 2023 ?

- LMC maladie réglée pour tout le monde ?

  - **NON** car
    - Il reste encore des quelques **progressions**: entre 5 et 10 % des patients
    - Il reste encore des **échecs**:

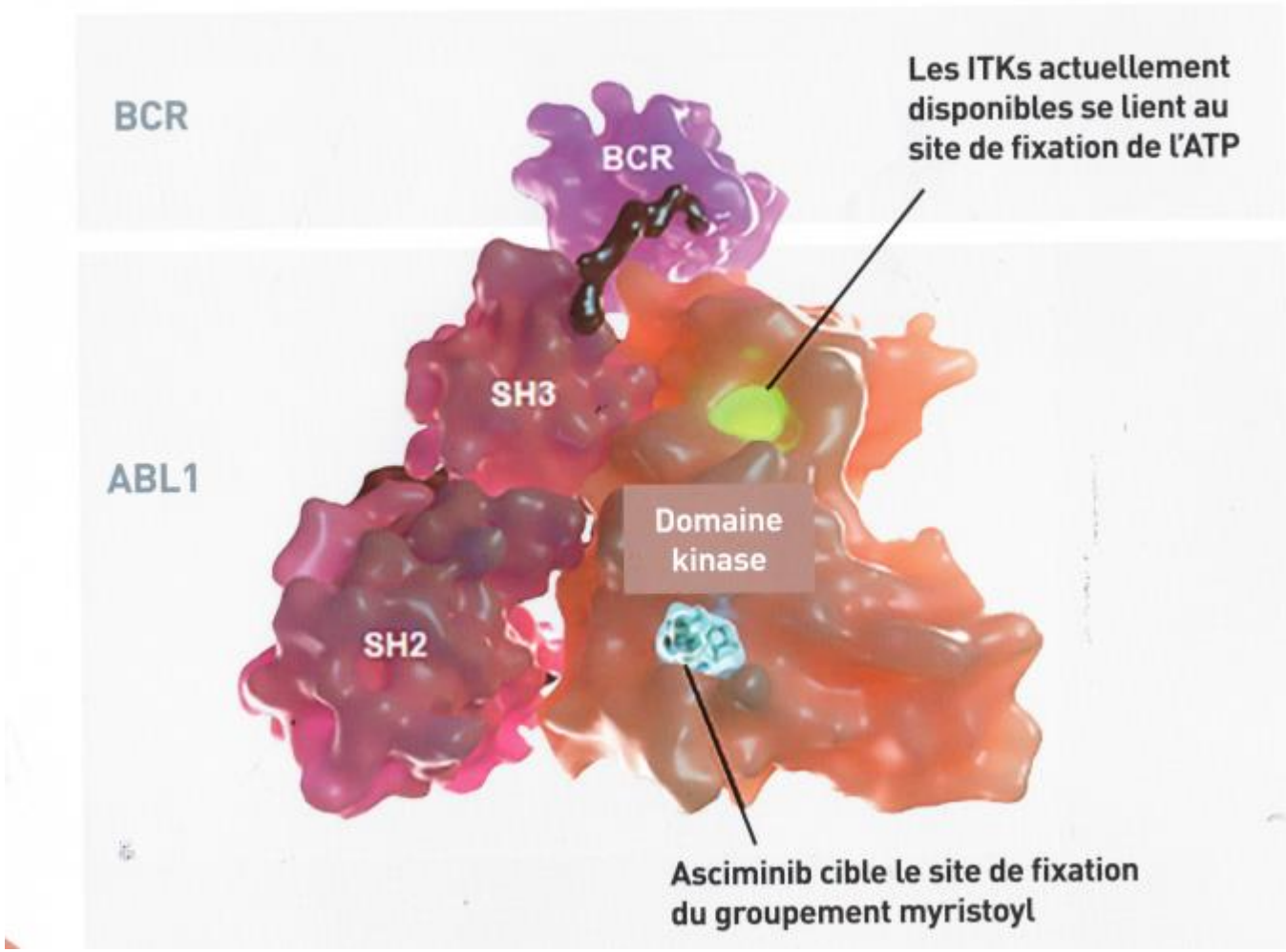
      il est estimé qu'environ 15 % des patients vont résister à un ITK en 2ème ligne
    - Il reste des **intolérances de classe**
    - Il reste des **EIG à gérer**: effets «off-target» sur le long terme

Reste donc un «medical needs »

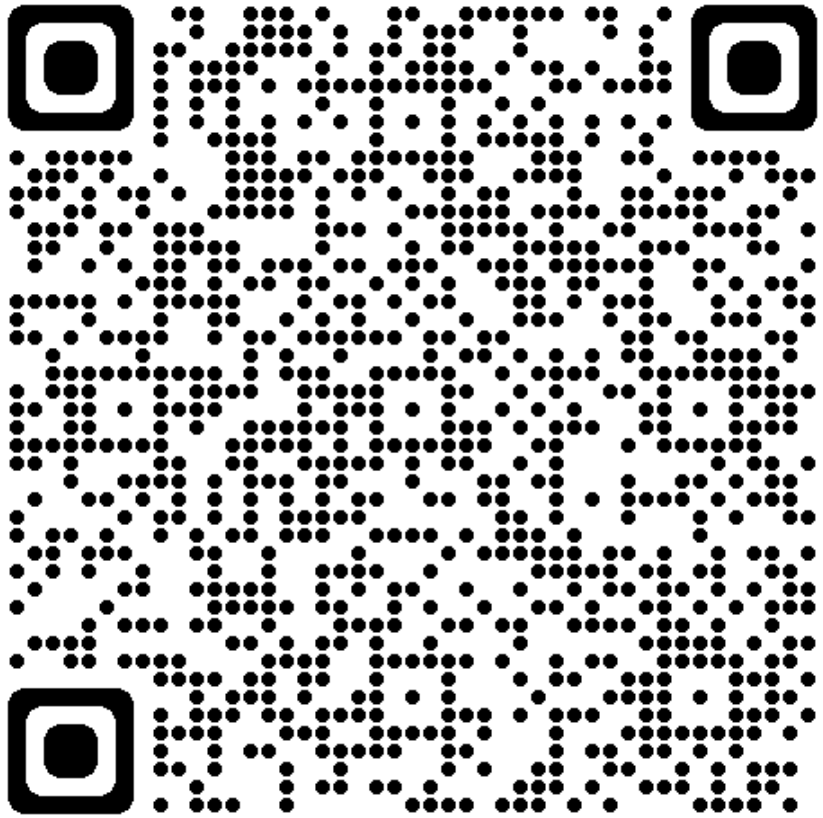
- Asciminib

- Nouvelle molécule: inh. STAMP
  - STAMP: **S**pecifically **T**argeting the **A**bl1 **M**yristoyl **P**ocket
  - Tout nouveau mécanisme d’action

NOUVEAU CIBLAGE SPECIFIQUE DE BCR::ABL1 PAR SCEMBLIX® (asciminib) [1,2]



Mécanisme d’action: à flasher please ! 3 mn



Mécanisme d’action

- https://www.professionnels.novartis.fr/node/918731?hash=cf8371f98689e762b05ea467955d111aad57cc400f6e77e8a8a4946515191961

Etude Ascembl

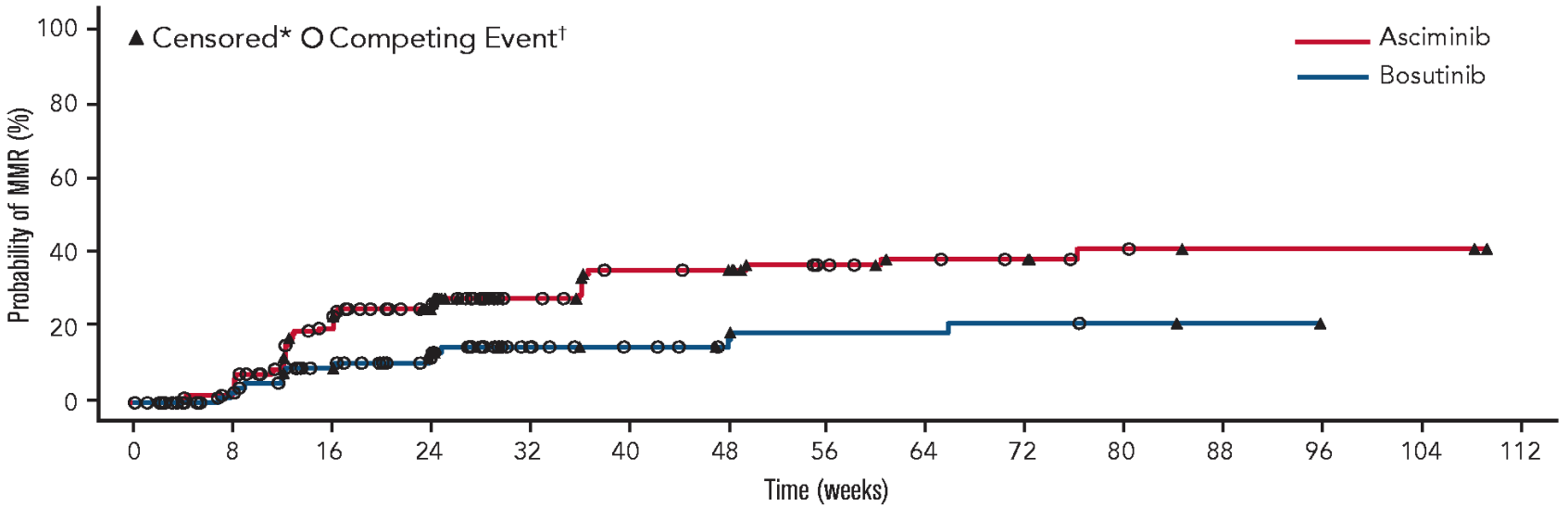
- Etude phase 3:
  - Asciminib vs Bosutinib
  - Random 2 : 1
  - Switch possible en cours

- Inclusion:
  - LMC-PC après 2 ITK
  - En échec ou intolérant
  - Pas de mutation T315I ou V299L
  - bcr::abl $\geq$ 0,1%

Etude Ascembl

- Critère principal
  - RMM à 24 semaines
  - RMM à 96 semaines
- Critères secondaires
  - RCCy

The cumulative incidence of MMR by **week 24** was 25.5% with asciminib vs 13,2% with bosutinib



Number of patients still at risk

Asciminib	157	152	145	129	107	92	85	55	45	41	28	28	25	19	17	14	12	11	10	5	4	3	2	2	2	2	2	0
Bosutinib	76	72	66	60	52	46	39	28	16	12	11	9	6	4	4	4	4	3	3	3	2	2	1	1	0	0	0	0	0

Cumulative number of competing events

Asciminib	0	5	8	14	17	23	27	35	44	46	47	47	48	48	50	52	52	53	54	55	55	56	56	56	56	56	56	56	56
Bosutinib	0	4	8	11	16	20	25	31	42	45	46	48	49	49	49	49	49	49	49	49	50	50	50	50	50	50	50	50	50

*Patients who did not achieve MMR were censored at their last molecular assessment date.
†Discontinuation from treatment for any reason, without prior achievement of MMR, is considered a competing event.

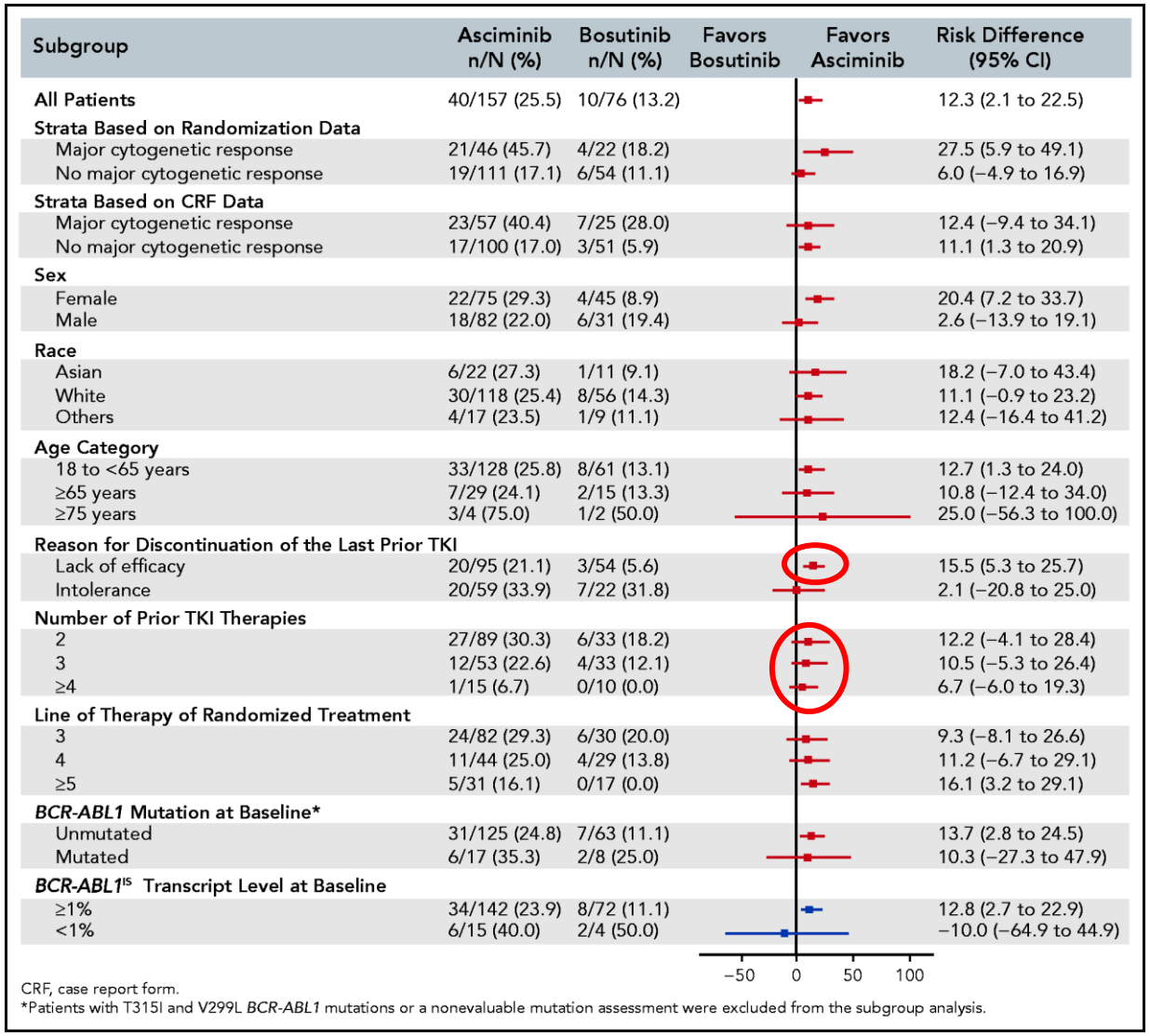
25,5%

13,2%

Réa D, blood 2021

Risk difference (95% CI) for MMR at week 24 from subgroup analyses

- Ascimib
  - Avantage quelque soit lignes ITK
  - Surtout si absence efficacité



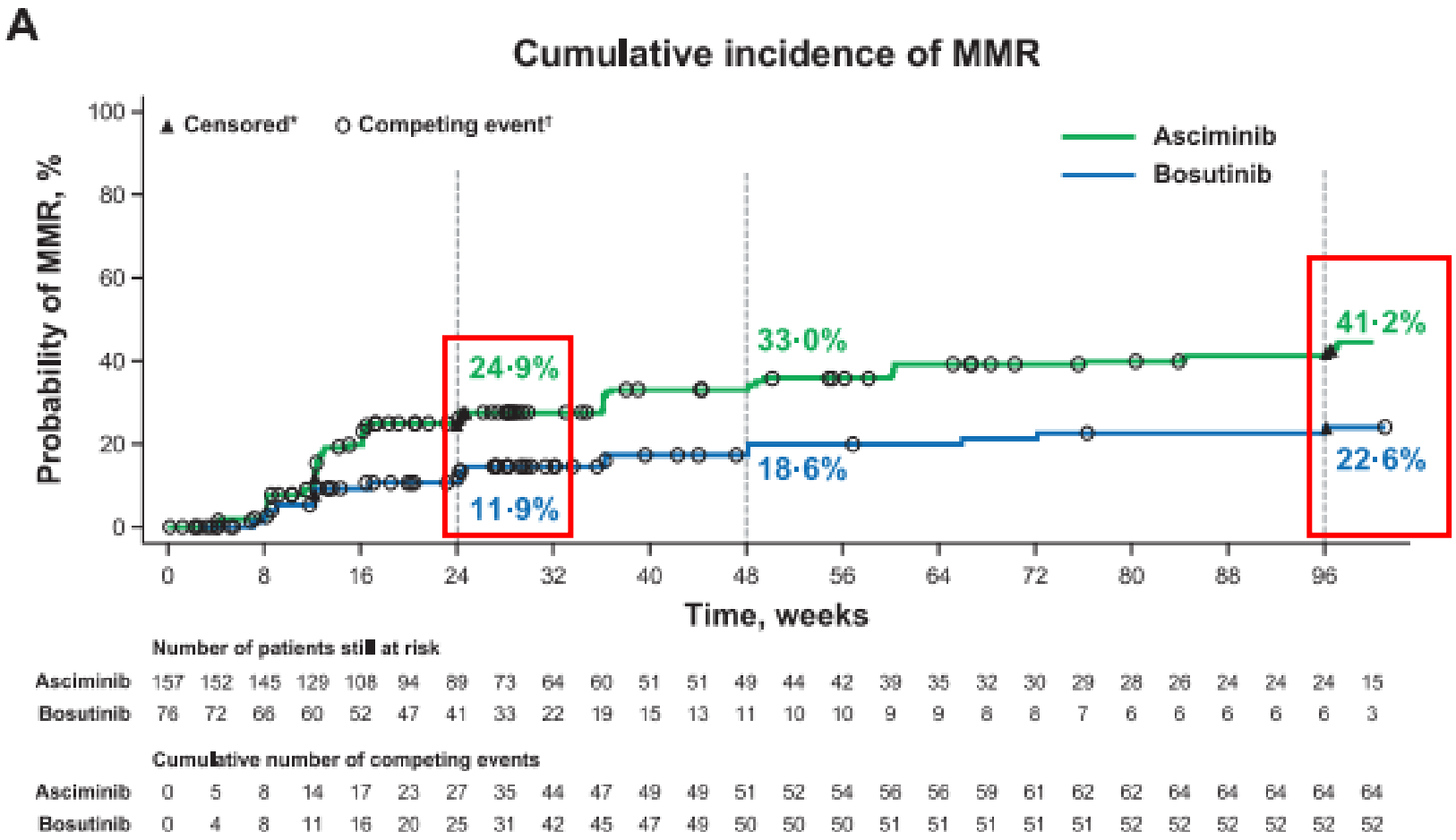
Réa D, blood 2021

CCyR at week 24 and 96

- The CCyR rate at week 24 in patients without CCyR at baseline was 40.8% with asciminib vs 24.2% with bosutinib

- At week 96: asciminib 39,8% vs 16,1% with bosutinib

The cumulative incidence of MMR by **week 96** was 41,2% with asciminib vs 22,6% with bosutinib



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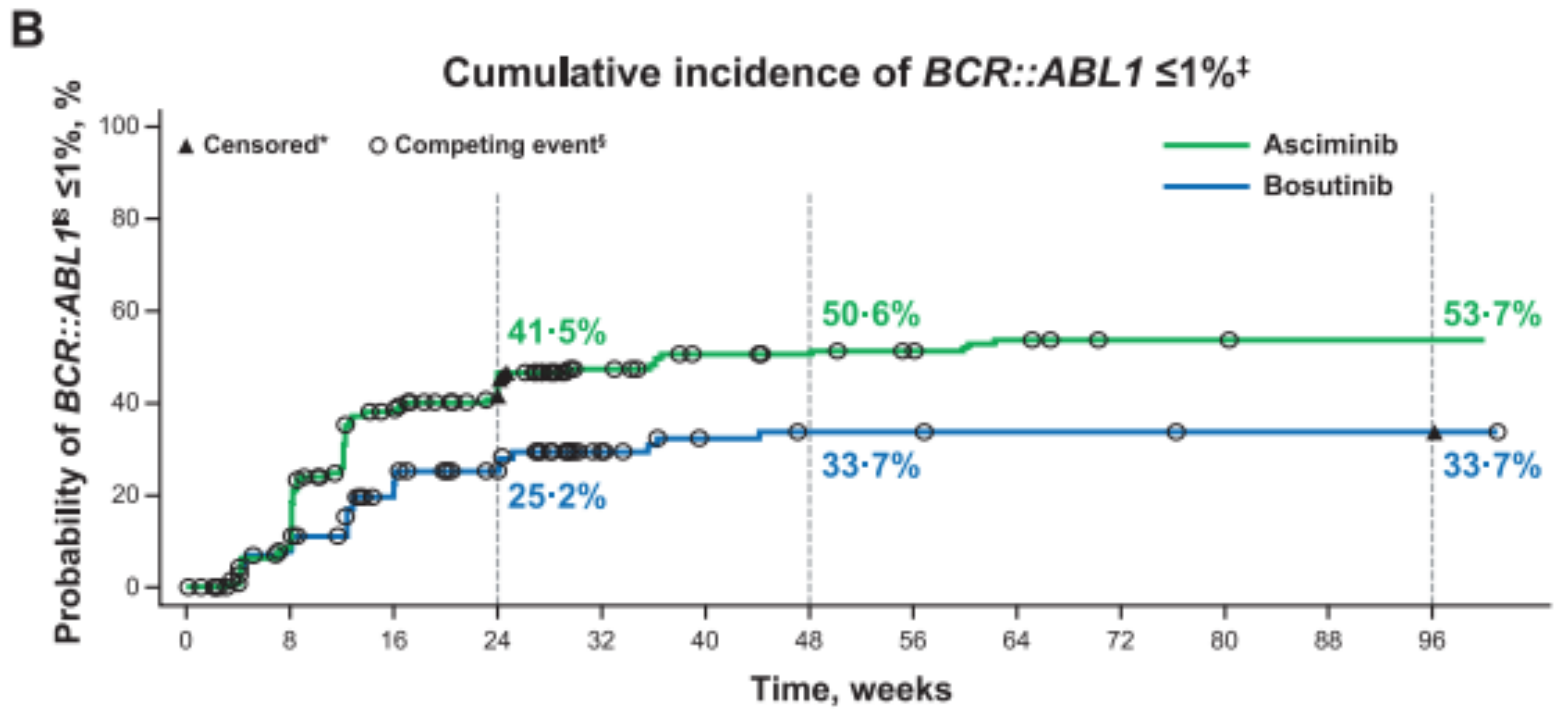

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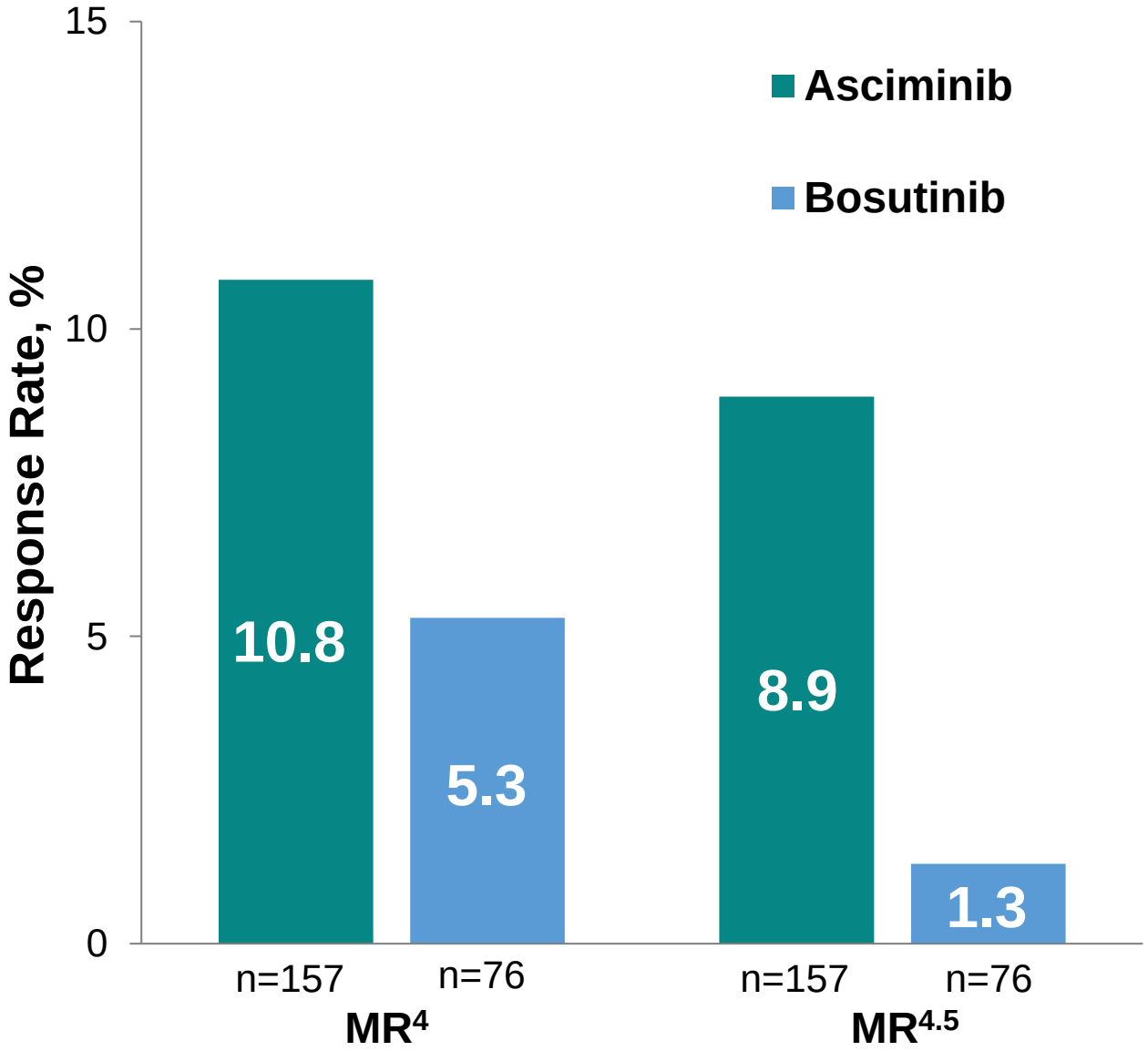
Taux de réponses moléculaires profondes

MR^4 and $MR^{4.5}$ Rates at 24 Weeks

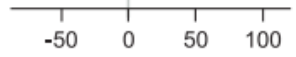


- At 24 weeks, more patients on asciminib than on bosutinib achieved MR^4 and $MR^{4.5}$
  - MR^4 or lower: 17 (10.8%) patients on asciminib vs 4 (5.3%) on bosutinib
  - $MR^{4.5}$: 14 (8.9%) patients on asciminib and 1 (1.3%) on bosutinib
- Rates of *BCR-ABL1*^{IS} ≤1% at week 24 among patients with *BCR-ABL1*^{IS} >1% at baseline:
  - Asciminib (n = 142): 44.5%
  - Bosutinib (n = 72): 22.2%

Risk difference (95% CI) for MMR at week 96 from subgroup analyses

- Ascimib
  - Confirmation
  - Avantage quelque soit lignes ITK
  - Surtout si absence efficacité

Subgroup	Asciminib, n/N (%)	Bosutinib, n/N (%)	Risk difference, % (95% CI)
All patients	59/157 (37·6)	12/76 (15·8)	21·8 (10·6 to 33·0)
Strata based on randomization data			
Major cytogenetic response	25/46 (54·4)	3/22 (13·6)	40·7 (20·4 to 61·0)
No major cytogenetic response	34/111 (30·6)	9/54 (16·7)	14·0 (0·8 to 27·1)
Sex			
Female	30/75 (40·0)	3/45 (6·7)	33·3 (20·1 to 46·6)
Male	29/82 (35·4)	9/31 (29·0)	6·3 (−12·7 to 25·4)
Race			
Asian	8/22 (36·4)	2/11 (18·2)	18·2 (−12·2 to 48·6)
White	44/118 (37·3)	9/56 (16·1)	21·2 (8·2 to 34·2)
Others	7/17 (41·2)	1/9 (11·1)	30·1 (−1·1 to 61·2)
Age category			
18 to <65 years	48/128 (37·5)	7/61 (11·5)	26·0 (14·4 to 37·6)
≥65 years	11/29 (37·9)	5/15 (33·3)	4·6 (−25·1 to 34·3)
≥75 years	4/4 (100)	1/2 (50·0)	50·0 (−19·3 to 100·0)
Reason for discontinuation of the last prior TKI			
Lack of efficacy	29/95 (30·5)	4/54 (7·4)	23·1 (11·5 to 34·7)
Intolerance	30/59 (50·9)	8/22 (36·4)	14·5 (−9·3 to 38·3)
Number of prior TKI therapies			
2	38/89 (42·7)	9/33 (27·3)	15·4 (−2·9 to 33·8)
3	19/53 (35·9)	3/33 (9·1)	26·8 (10·5 to 43·0)
≥4	2/15 (13·3)	0/10 (0·0)	13·3 (−3·9 to 30·5)
Line of therapy of randomized treatment			
3	34/82 (41·5)	9/30 (30·0)	11·5 (−8·1 to 31·0)
4	16/44 (36·4)	3/29 (10·3)	26·0 (8·0 to 44·0)
≥5	9/31 (29·0)	0/17 (0·0)	29·0 (13·1 to 45·0)
BCR::ABL1* mutations at baseline			
Not detected	47/125 (37·6)	10/63 (15·9)	21·7 (9·3 to 34·1)
Detected	7/17 (41·2)	2/8 (25·0)	16·2 (−21·9 to 54·2)
***BCR::ABL1*[IS] transcript level at baseline**			
≥1%	49/142 (34·5)	10/72 (13·9)	20·6 (9·4 to 31·8)
<1%	10/15 (66·7)	2/4 (50·0)	16·7 (−37·8 to 71·2)



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Etude Ascembl

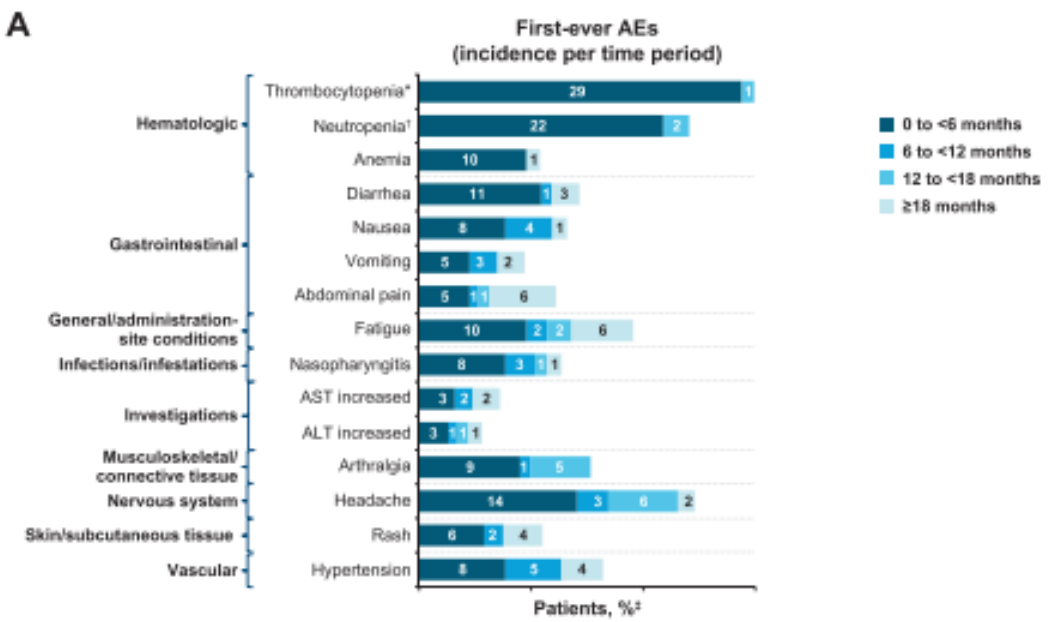
- Toxicités Asciminib
  - Thrombopénie 29%
  - HTA 13,5%

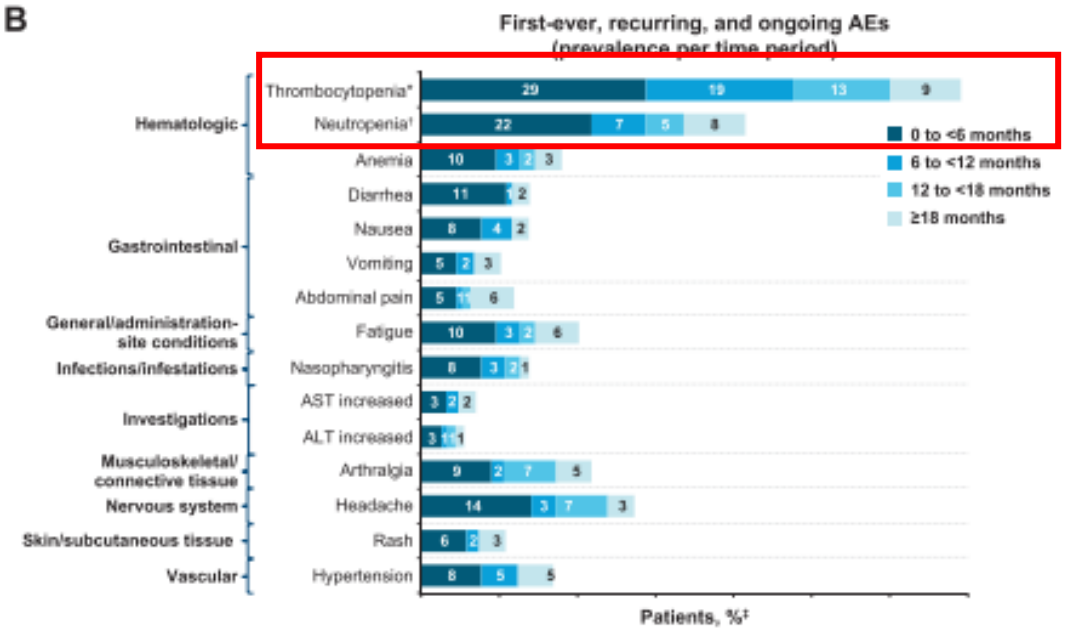
- Toxicités Bosutinib
  - Diarrhées 72,4%

Table 2. Adverse events regardless of relationship to study drug (reported in ≥5% of patients in any treatment arm).

Event, *n* (%)[a]	Asciminib 40 mg twice daily (*n* = 156)		Bosutinib 500 mg once daily (*n* = 76)	
	All grades	Grade ≥ 3	All grades	Grade ≥ 3
Number of patients with ≥1 adverse event	142 (91.0)	88 (56.4)	74 (97.4)	52 (68.4)
Thrombocytopenia[b]	46 (29.5)	35 (22.4)	15 (19.7)	7 (9.2)
Neutropenia[c]	36 (23.1)	29 (18.6)	16 (21.1)	11 (14.5)
Headache	31 (19.9)	3 (1.9)	12 (15.8)	0
Fatigue	23 (14.7)	1 (0.6)	7 (9.2)	1 (1.3)
Hypertension	21 (13.5)	10 (6.4)	4 (5.3)	3 (3.9)
Arthralgia	20 (12.8)	1 (0.6)	3 (3.9)	0
Diarrhea	20 (12.8)	0	55 (72.4)	8 (10.5)
Nausea	18 (11.5)	1 (0.6)	35 (46.1)	0
Nasopharyngitis	17 (10.9)	0	3 (3.9)	0
Anemia	16 (10.3)	2 (1.3)	6 (7.9)	3 (3.9)
Abdominal pain	14 (9.0)	0	12 (15.8)	1 (1.3)
Pain in extremity	14 (9.0)	1 (0.6)	5 (6.6)	0
Rash	14 (9.0)	0	18 (23.7)	3 (3.9)
Asthenia	13 (8.3)	0	1 (1.3)	0
Cough	13 (8.3)	0	5 (6.6)	0
Back pain	12 (7.7)	1 (0.6)	3 (3.9)	1 (1.3)
Vomiting	12 (7.7)	2 (1.3)	20 (26.3)	0
Dizziness	11 (7.1)	0	2 (2.6)	0
Dyspepsia	11 (7.1)	0	3 (3.9)	0
Insomnia	11 (7.1)	0	1 (1.3)	0
Peripheral edema	11 (7.1)	0	2 (2.6)	0
Upper respiratory tract infection	11 (7.1)	1 (0.6)	4 (5.3)	0
Myalgia	10 (6.4)	0	2 (2.6)	0
Amylase increased	9 (5.8)	1 (0.6)	4 (5.3)	0
Aspartate aminotransferase increased	9 (5.8)	3 (1.9)	16 (21.1)	5 (6.6)
Muscle spasms	9 (5.8)	1 (0.6)	0	0
Constipation	8 (5.1)	0	4 (5.3)	0
Decreased appetite	8 (5.1)	0	6 (7.9)	0
Dry skin	8 (5.1)	0	6 (7.9)	0
Dyspnea	8 (5.1)	0	4 (5.3)	0
Lipase increased	8 (5.1)	6 (3.8)	5 (6.6)	4 (5.3)
Non-cardiac chest pain	8 (5.1)	2 (1.3)	1 (1.3)	0
Oropharyngeal pain	8 (5.1)	0	2 (2.6)	0
Pruritus	8 (5.1)	0	5 (6.6)	1 (1.3)
Rash maculopapular	8 (5.1)	0	2 (2.6)	1 (1.3)
Abdominal pain upper	7 (4.5)	0	5 (6.6)	1 (1.3)
Alanine aminotransferase increased	7 (4.5)	1 (0.6)	23 (30.3)	11 (14.5)
Pyrexia	6 (3.8)	2 (1.3)	6 (7.9)	1 (1.3)
Blood creatinine increased	5 (3.2)	0	5 (6.6)	0
Influenza-like illness	3 (1.9)	0	4 (5.3)	0
Hypophosphatemia	2 (1.3)	1 (0.6)	4 (5.3)	3 (3.9)

Toxicités Asciminib





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Ascembl

- EI de spécial intérêt
  - Effet cardiaque ?

Table 3. EAIRs of adverse events of special interest.

EAIR, *n* (per 100 patient-treatment years)[a,b]	Asciminib 40 mg twice daily (*n* = 156)	Bosutinib 500 mg once daily (*n* = 76)
Cardiac failure (clinical events)	3 (1.1)	1 (1.3)
Edema and fluid retention	16 (6.4)	7 (10.1)
Gastrointestinal toxicity	52 (26.6)	60 (319.2)
Hemorrhage	19 (7.4)	8 (11.1)
Hepatotoxicity (including AEs related to laboratory value abnormalities)	17 (6.8)	25 (40.8)
Hypersensitivity[c]	32 (14.0)	26 (48.2)
Pancreatic toxicity	13 (5.1)	7 (10.2)
QTc prolongation	6 (2.3)	1 (1.3)
Reproductive toxicity[d]	3 (1.1)	1 (1.3)

EAIR exposure-adjusted incidence rate.

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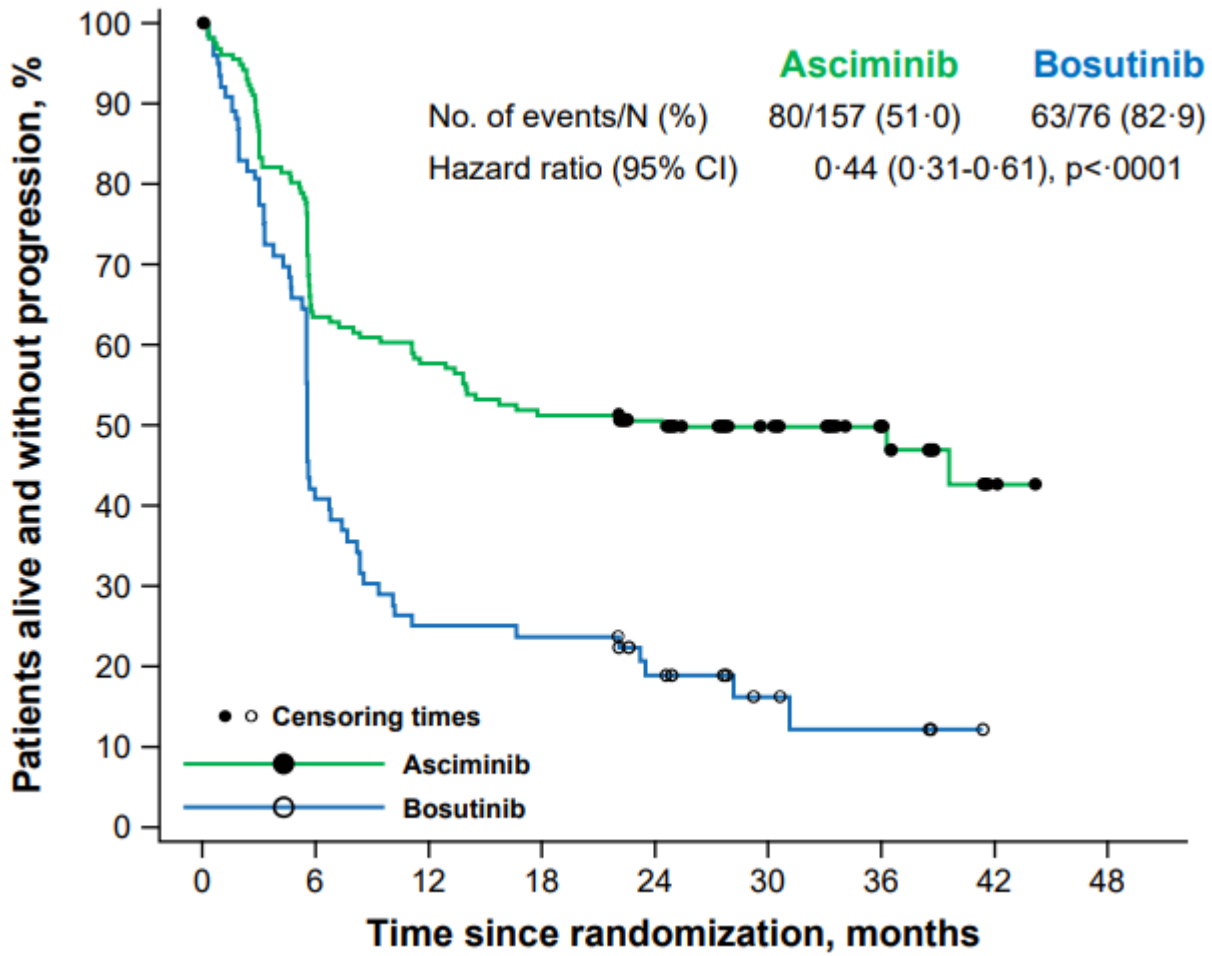
PFS


Asciminib
Bosutinib
No. of events/N (%)
80/157 (51·0)
63/76 (82·9)
Hazard ratio (95% CI)
0·44 (0·31-0·61), p<·0001
Patients alive and without progression, %
100
90
80
70
60
50
40
30
20
10
0
Censoring times
Asciminib
Bosutinib
0
6
12
18
24
30
36
42
48
Time since randomization, months

Conclusion Ascembl

- Collectively, these updated results from ASCEMBL are a confirmation of the enduring clinical benefit of asciminib after longer exposure and continue to illustrate that asciminib has transformed CML treatment as a new standard of care for patients with CML-CP treated with ≥2 prior TKIs and support its ongoing development in earlier lines of therapy

Asciminib développement

Asciminib en 1ère ligne: Asciminib monoT

- Etude ASCEND IIT: Asciminib
- Etude ASC4First: Asciminib vs autres ITK
- Etude ASC4Start: Asciminib vs Nilotinib

Asciminib en 1ère ligne: Asciminib association avec Imatinib

- Etude Asc4More: Asciminib + Imatinib si Sub optimal

Asciminib dans LMC T315I

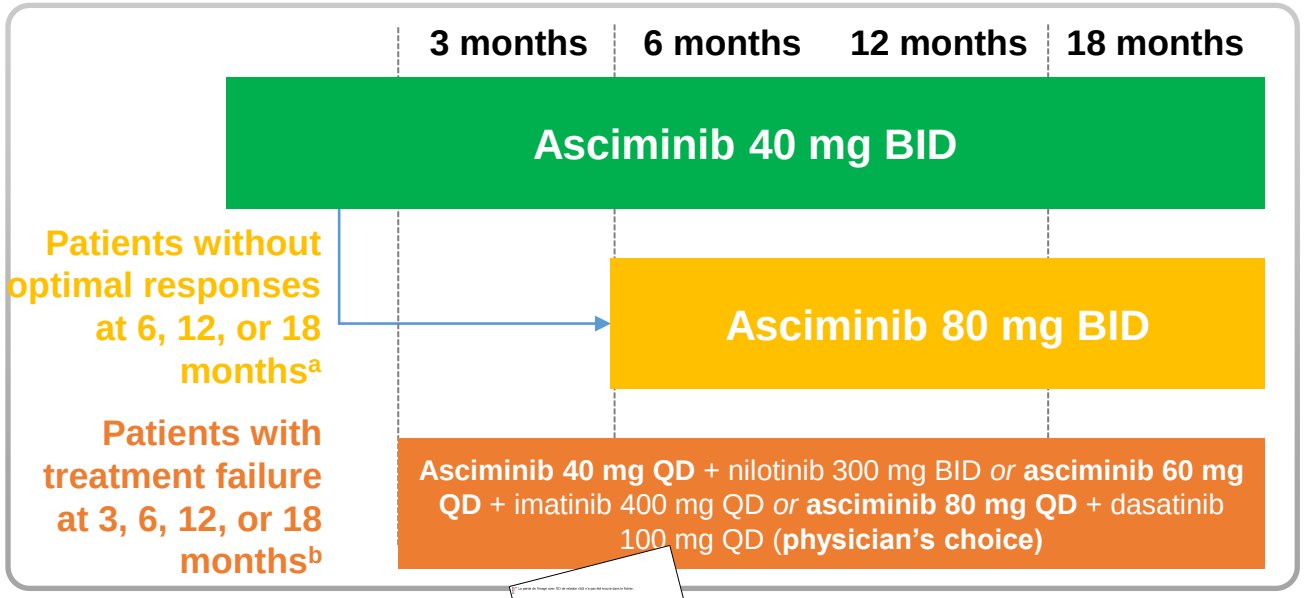
Novartis Oncology

ASCEND IIT : Asciminib in 1st line

This resource is associated with abstract 79 at ASH 2022

Disposition

Study design and interim analysis



Co-primary endpoints: EMR or *BCR::ABL1*^{IS} ≤10% at 3 months and MMR by 12 months

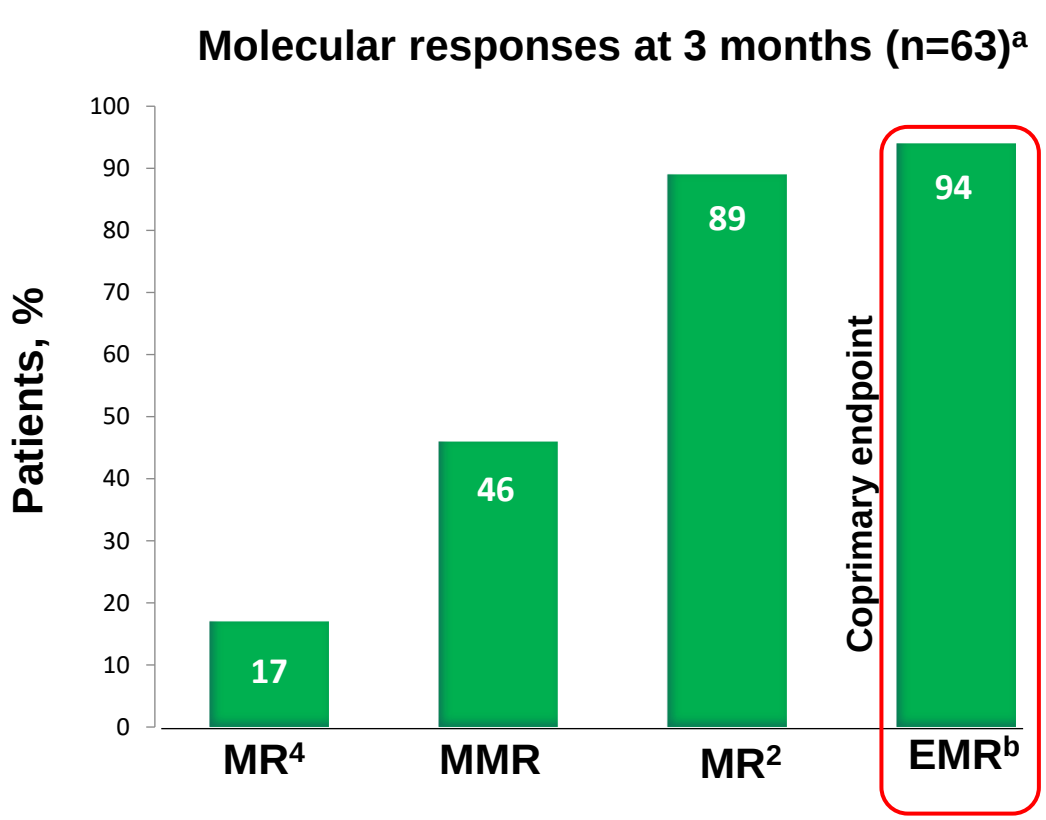
Protocol-specified interim analysis: EMR at 3 months
Data cutoff: July 15th, 2022

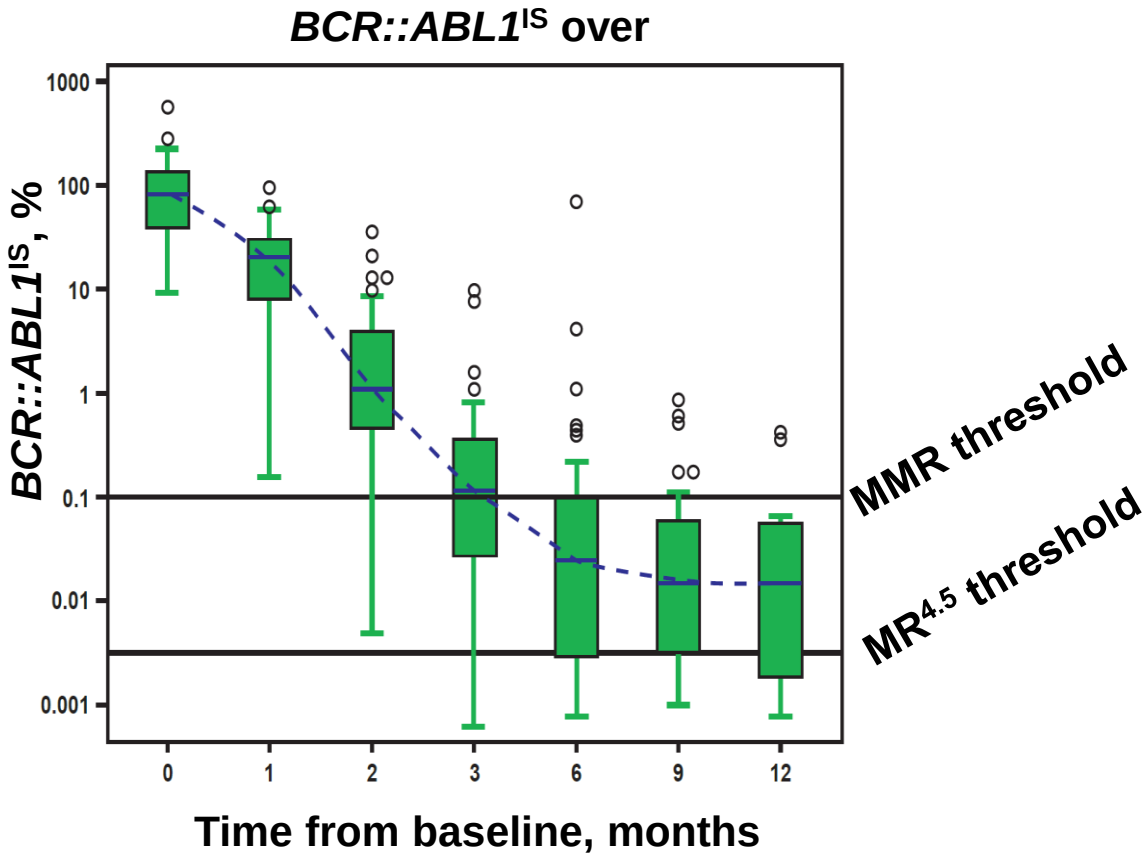
Median follow-up: 10 months

- **79/100 patients** were registered by the data cutoff[c]
- **3 patients with suboptimal response** (per 2020 ELN recommendations)[a] underwent dose escalation
- **9 patients discontinued** treatment due to AEs (n=5)[d], withdrawal of consent (n=1), loss to follow up (n=1), and asciminib resistance (n=2)[e]

[b] *BCR::ABL1*^{IS} >10% at 3 or 6 months and *BCR::ABL1*^{IS} >1% at 12 or 18 months.
[c] ASCEND will enroll ≈100 patients over 15 Australian and New Zealand sites.
[d] Included persistent grade 4 cytopenia requiring HSCT (n=1) and recurrent asymptomatic lipase elevations (n=4).
[e] 1 due to loss of MMR at 9 months after reaching a nadir of 0.067% at 6 months without evidence of kinase domain or myristoyl pocket mutations and 1 due to transformation to CML-BP at 6 months with myristoyl pocket mutations A337T (40%), A337V (10%), and P465S (10%), having previously achieved *BCR::ABL1*^{IS} of 0.37% at 3 months.
Yeung DT, et al. ASH2022 Annual Meeting; December 10-13, 2022; New Orleans, LA, and virtual. Abstract 79.

Molecular responses at 3 months and *BCR::ABL1*^{IS} over time with asciminib





- **59 of 63** evaluable patients **(or 94%)** receiving **asciminib achieved EMR**
- A **high proportion of deep molecular responses were achieved at 3 months** with **asciminib**. **Of 63** evaluable patients, **89% achieved MR^2, 46% achieved MMR**, and **17% achieved MR^4 or better**

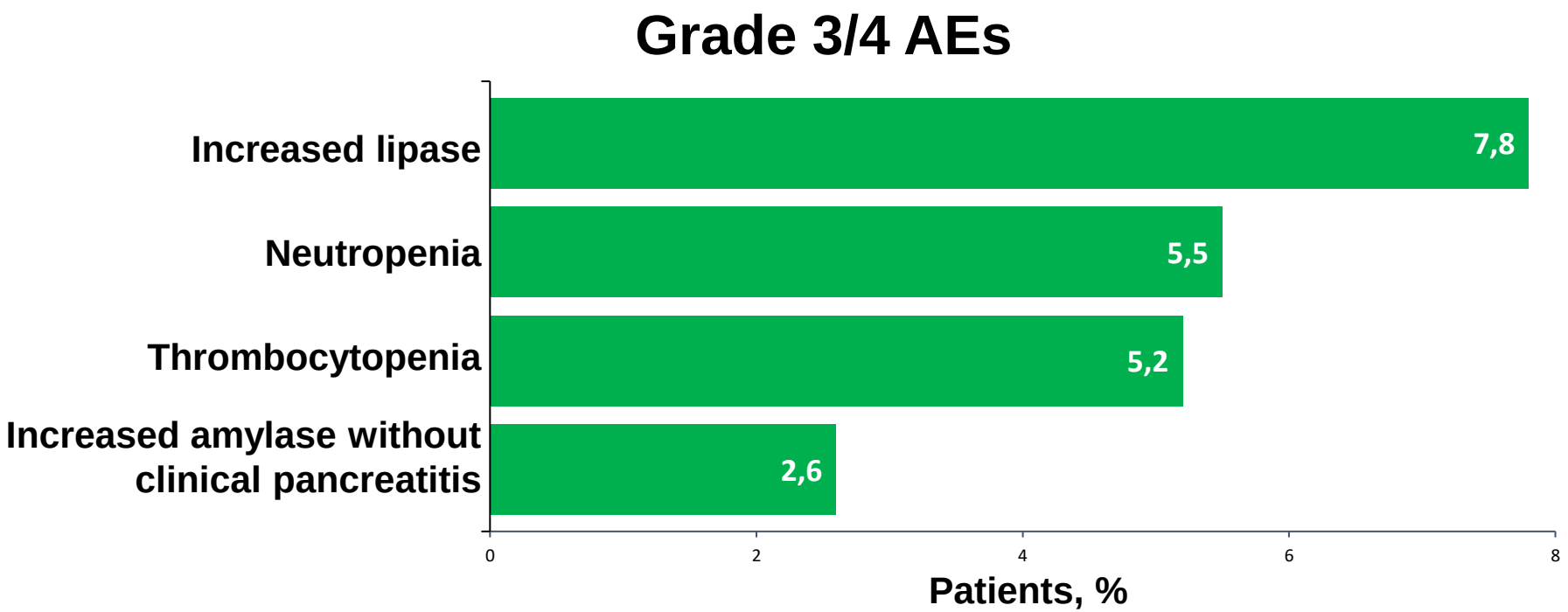
MR^2, *BCR::ABL1*^{IS} ≤1%; MR^4, *BCR::ABL1*^{IS} ≤0.01%; MR$^{4.5}$, *BCR::ABL1*^{IS} ≤0.0032%.

[a] All patients with 3 months of follow-up were included in this analysis.

[b] Four patients were nonresponders: 1 missed this assessment and 3 withdrew from the study by this time point.

Yeung DT, et al. ASH2022 Annual Meeting; December 10-13, 2022; New Orleans, LA, and virtual. Abstract 79.

Most frequent grade 3/4 AEs

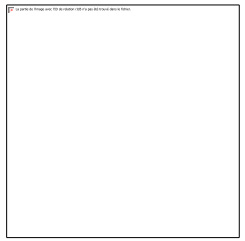


- Other **grade 3 AEs included increased AST, increased ALT, anemia, back pain, abdominal pain, and infection**, each reported once

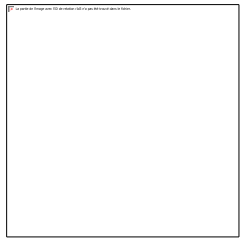
ALT, alanine aminotransferase; AST, aspartate aminotransferase.

Yeung DT, et al. ASH2022 Annual Meeting; December 10-13, 2022; New Orleans, LA, and virtual. Abstract 79.

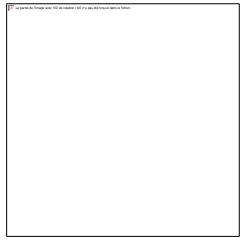
ASCEND abstract conclusions



After a median follow-up of 10 months, **asciminib** demonstrated **promising efficacy and favorable tolerability** as frontline treatment for patients with CML-CP



Most patients achieved **EMR**, **nearly half achieved MMR**, and **many achieved MR^4 or better at 3 months**, supporting the potential for **treatment-free remission** with **asciminib**

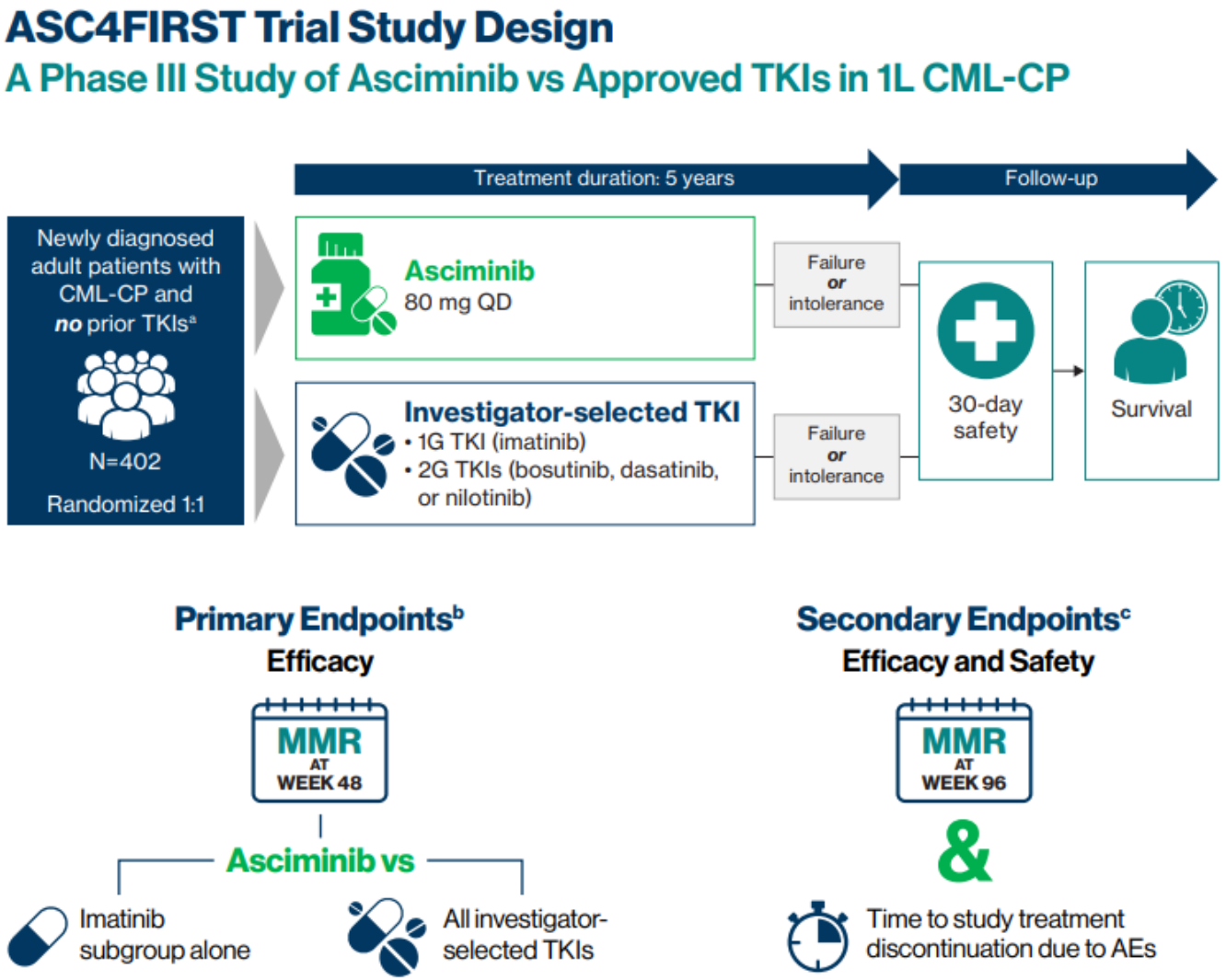


Safety results were encouraging with the **most common AEs being cytopenias and lipase elevations**, which appear to be ABL1 inhibitor class effects

CML-CP, chronic myeloid leukemia in chronic phase.

Yeung DT, et al. ASH2022 Annual Meeting; December 10-13, 2022; New Orleans, LA, and virtual. Abstract 79.

ASC4FIRST: A Phase III Study of Asciminib vs Investigator-Selected Tyrosine Kinase Inhibitor in Patients with Newly Diagnosed Chronic Myeloid Leukemia in Chronic Phase (CML-CP)



Hugues T, ASH 2022

Asc4First study

Key Inclusion Criteria

- Adults with CML-CP
- CML-CP within 3 months of diagnosis that meets ELN criteria[6]
- ECOG performance status of 0 or 1
- Typical BCR-ABL1 transcript at screening

Key Exclusion Criteria

- Previous treatment with anticancer agents[a,d]
- Impaired cardiac function or repolarization abnormality
- Cytopathologically confirmed CNS infiltration
- History of acute[e]/chronic pancreatitis
- History of acute/chronic liver disease

Will enroll ≈402 patients

in

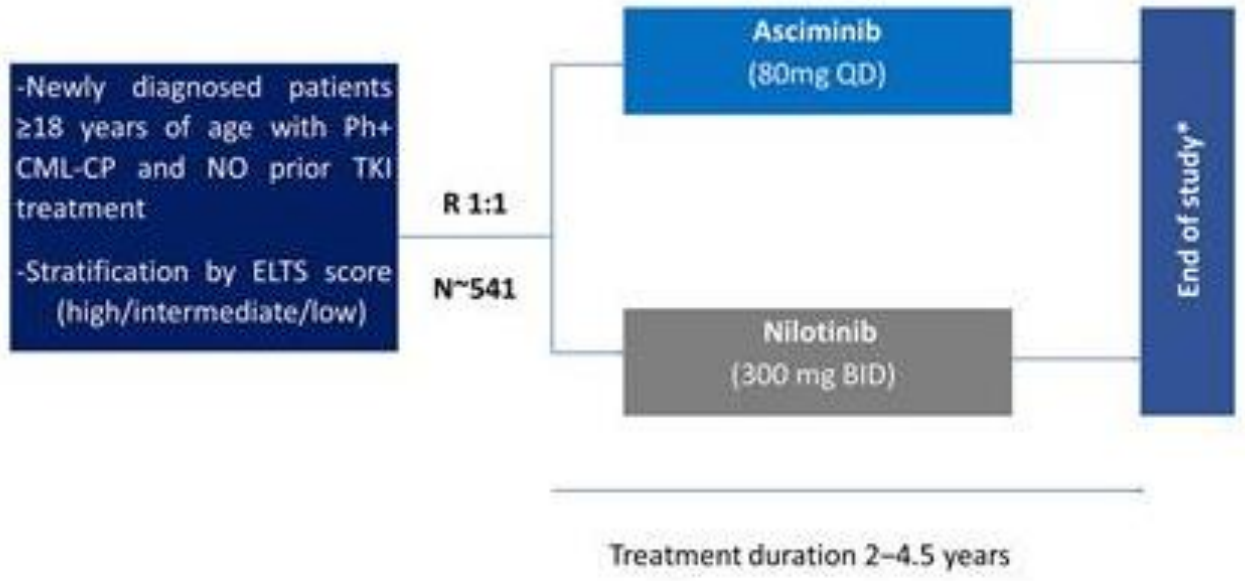
161 sites

in

31 countries

Etude en cours

ASC4START: A Phase IIIb, Open-Label, Randomized Study of Tolerability and Efficacy of Asciminib Versus Nilotinib in Patients with Newly Diagnosed Philadelphia Chromosome-Positive Chronic Myelogenous Leukemia in Chronic Phase



Etude en cours

Hochhaus A, ASH 2022

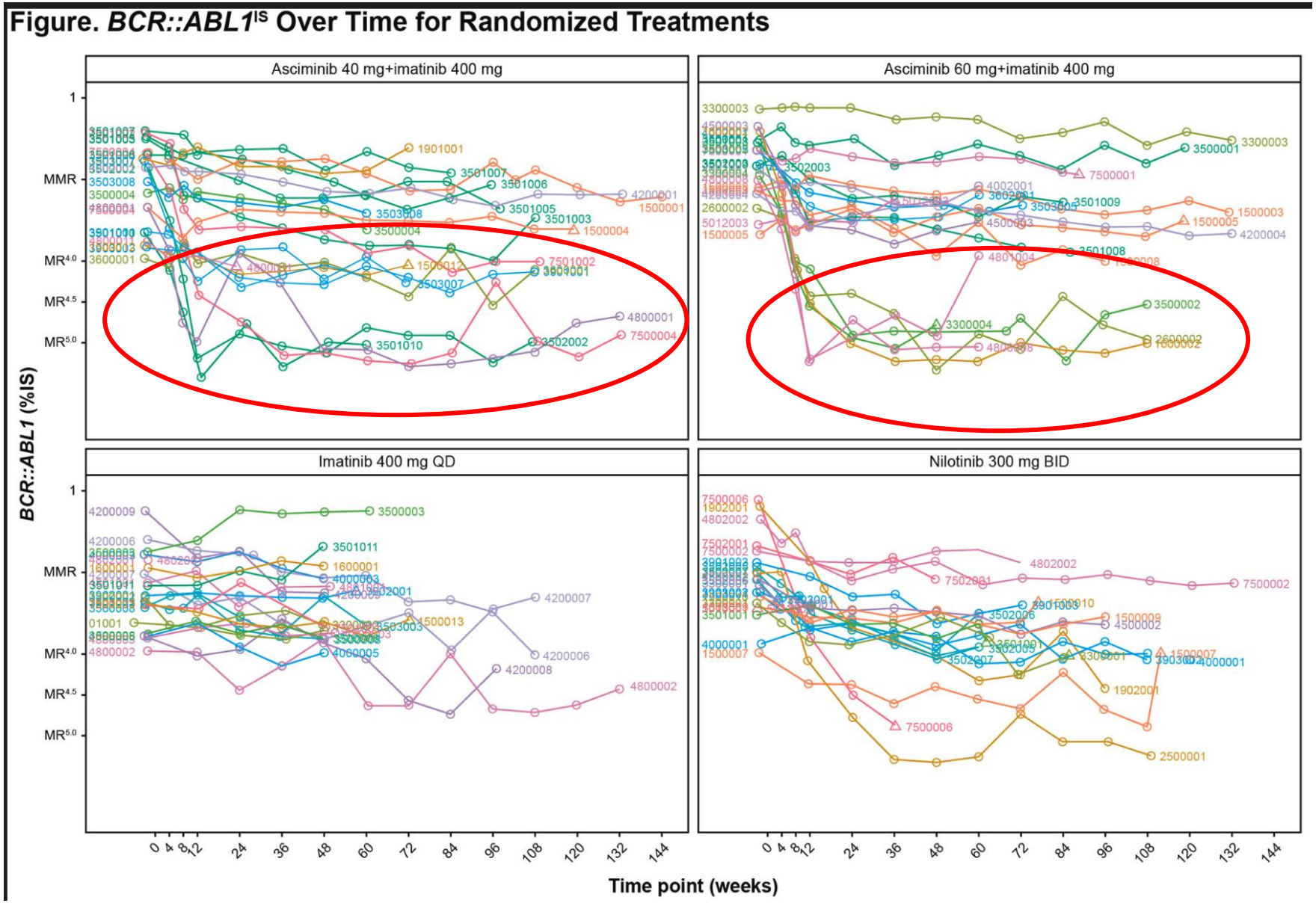
Efficacy and Safety Results from ASC4MORE, a Randomized Study of Asciminib (ASC) Add-on to Imatinib (IMA), Continued IMA, or Switch to Nilotinib (NIL) in Patients (Pts) with Chronic-Phase Chronic Myeloid Leukemia (CML-CP) Not Achieving Deep Molecular Responses (DMRs) with ≥1 Year of IMA

• Randomisation	RM4 at W48
• Asciminib 40 mg + Imatinib 400 mg	42,9%
• Asciminib 60 mg + Imatinib 400 mg	28,6%
• Imatinib 400 mg	0%
• Nilotinib 300 mg x2	23,8%

Cortes J ASH 2022

Asc4more

% patients RM profonde
plus importante
Avec l'association →



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Asc4more: tolérance

Conclusion: Association prometteuse

Table. AEs by Preferred Term (≥2 Pts in Any Treatment Arm)

Preferred term	Asciminib 40 mg QD + IMA n=21		Asciminib 60 mg QD + IMA n=21		IMA 400 mg QD n=20		NIL 300 mg BID n=21	
	All grade n (%)	Grade ≥3 n (%)	All grade n (%)	Grade ≥3 n (%)	All grade n (%)	Grade ≥3 n (%)	All grade n (%)	Grade ≥3 n (%)
Pts with ≥1 event	20 (95.2)	7 (33.3)	19 (90.5)	7 (33.3)	14 (70.0)	1 (5.0)	21 (100)	9 (42.9)
Alopecia	2 (9.5)	0	3 (14.3)	0	0	0	1 (4.8)	0
Dry skin	2 (9.5)	0	3 (14.3)	0	0	0	0	0
Lipase increased	3 (14.3)	0	3 (14.3)	1 (4.8)	3 (15.0)	0	2 (9.5)	2 (9.5)
Nausea	7 (33.3)	0	3 (14.3)	0	2 (10.0)	0	3 (14.3)	0
Blood creatine phosphokinase increased	1 (4.8)	0	2 (9.5)	1 (4.8)	2 (10.0)	0	1 (4.8)	0
Blood creatinine increased	2 (9.5)	0	2 (9.5)	0	0	0	0	0
COVID-19	3 (14.3)	0	2 (9.5)	0	2 (10.0)	0	3 (14.3)	1 (4.8)
Diarrhea	5 (23.8)	0	2 (9.5)	1 (4.8)	3 (15.0)	0	1 (4.8)	0
Fatigue	3 (14.3)	1 (4.8)	2 (9.5)	0	0	0	2 (9.5)	0
Hypophosphatemia	2 (9.5)	0	2 (9.5)	0	3 (15.0)	1 (5.0)	1 (4.8)	0
Alanine aminotransferase increased	1 (4.8)	0	1 (4.8)	0	0	0	5 (23.8)	0
Amylase increased	1 (4.8)	0	1 (4.8)	0	2 (10.0)	0	1 (4.8)	1 (4.8)
Aspartate aminotransferase increased	0	0	1 (4.8)	0	0	0	3 (14.3)	0
Back pain	0	0	1 (4.8)	0	0	0	2 (9.5)	2 (9.5)
Blood cholesterol increased	0	0	1 (4.8)	0	0	0	3 (14.3)	0
Blood phosphorus decreased	2 (9.5)	0	1 (4.8)	0	0	0	0	0
Headache	3 (14.3)	0	1 (4.8)	0	0	0	2 (9.5)	0
Hypokalemia	2 (9.5)	1 (4.8)	1 (4.8)	0	0	0	0	0
Myalgia	5 (23.8)	1 (4.8)	1 (4.8)	0	1 (5.0)	0	2 (9.5)	0
Neutropenia	2 (9.5)	2 (9.5)	1 (4.8)	0	0	0	0	0
Pancreatitis	1 (4.8)	0	1 (4.8)	1 (4.8)	0	0	2 (9.5)	0
Paresthesia	0	0	1 (4.8)	0	2 (10.0)	0	0	0
Pruritus	4 (19.0)	0	1 (4.8)	0	0	0	2 (9.5)	0
Rash	2 (9.5)	0	1 (4.8)	0	1 (5.0)	0	8 (38.1)	1 (4.8)
Urinary tract infection	3 (14.3)	1 (4.8)	1 (4.8)	0	1 (5.0)	0	0	0
Vomiting	2 (9.5)	1 (4.8)	1 (4.8)	0	2 (10.0)	0	1 (4.8)	0
Abdominal pain	0	0	0	0	0	0	2 (9.5)	0
Abdominal pain upper	2 (9.5)	2 (9.5)	0	0	0	0	2 (9.5)	0
Blood bilirubin increased	1 (4.8)	0	0	0	0	0	3 (14.3)	0
Conjunctivitis	2 (9.5)	0	0	0	1 (5.0)	0	0	0
Constipation	1 (4.8)	0	0	0	1 (5.0)	0	3 (14.3)	0
Dizziness	1 (4.8)	0	0	0	0	0	2 (9.5)	0
Folliculitis	0	0	0	0	0	0	3 (14.3)	0
Gamma-glutamyltransferase increased	1 (4.8)	0	0	0	0	0	2 (9.5)	1 (4.8)
Gilbert syndrome	0	0	0	0	0	0	3 (14.3)	2 (9.5)
Hyperglycemia	0	0	0	0	0	0	2 (9.5)	0
Hypertension	1 (4.8)	0	0	0	1 (5.0)	0	4 (19.0)	2 (9.5)
Hypertriglyceridemia	2 (9.5)	0	0	0	0	0	0	0
Hypocalcemia	0	0	0	0	2 (10.0)	0	0	0
Muscle spasms	2 (9.5)	0	0	0	1 (5.0)	0	1 (4.8)	0
Tinnitus	2 (9.5)	0	0	0	0	0	0	0

Cortes J ASH 2022

Asciminib dans LMC T315I

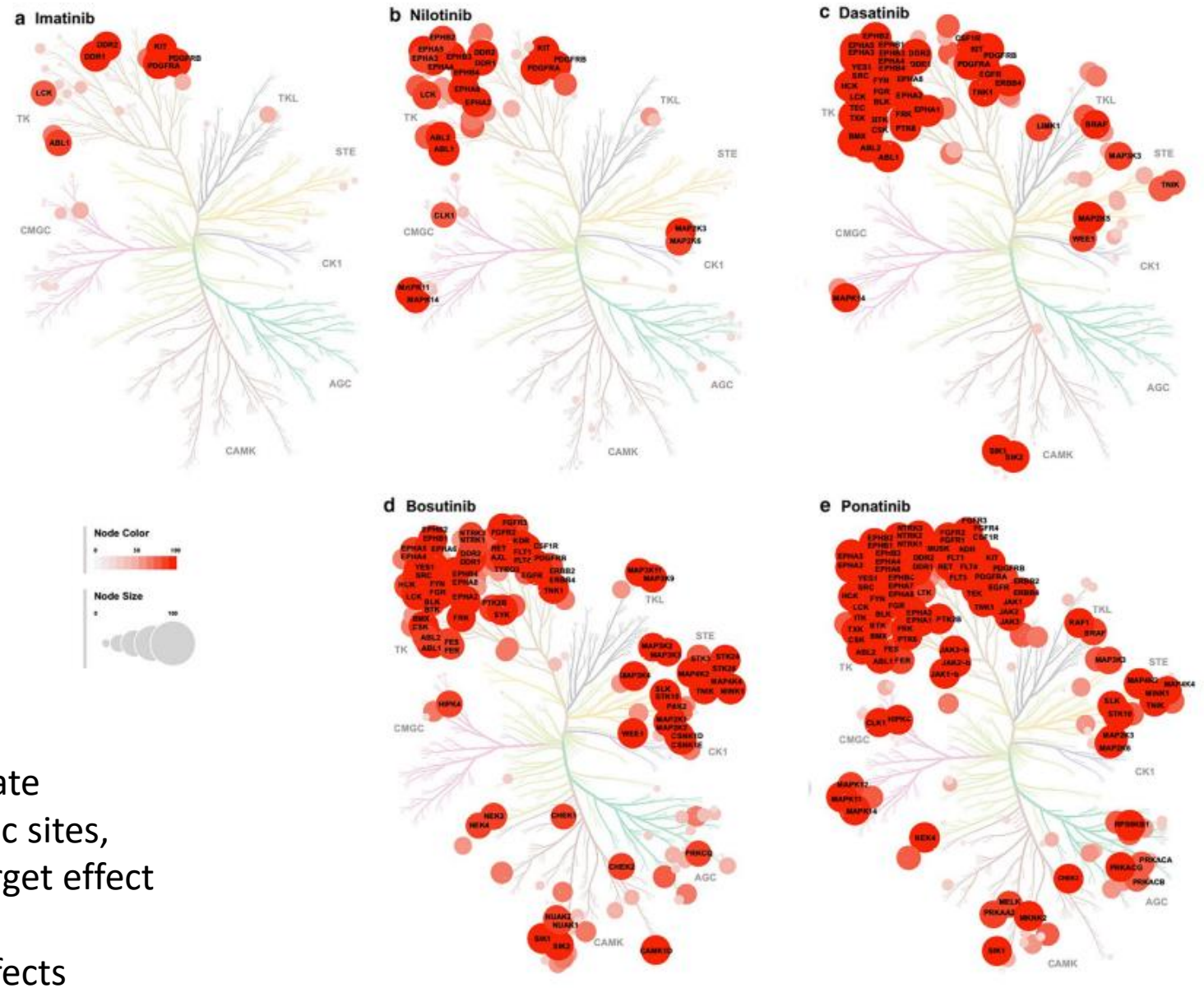
- Posologie requise 200 mg/j

- N = 48
  - 60% avait reçu Ponatinib

- RMM at W24 42%
- RMM at W96 48,9%

- Tolérance : idem dose 80 mg/j.

Inhibitions des kinases par ITK responsables des effets « off-target »



As it specifically binds to the myristate pocket, rather than other orthosteric sites, asciminib has a highly specifc on-target effect against the ABL1 kinase
without any significant off target effects

Lee H Int J Hematol 2021

conclusion

- Asciminib: nouvelle molécule et mode d'action nouveau
- Résultats très prometteur dès la 3ème ligne
- Résultats très prometteurs en 1ère ligne et en association
- Molécule qui va challenger le Ponatinib +++ car peu d'effets off-target

- Attention: déjà des mutations de résistances décrites.