Como o meu objetivo pode influenciar a terapia de primeira linha na LMC?

Carla Boquimpani

Grupo Oncoclínicas / HEMORIO

Nenhum conflito de interesse

Aos 20 anos .....

Aos 50 anos .....

Aos 70 anos .....

O tratamento da LMC tem que ser personalizado

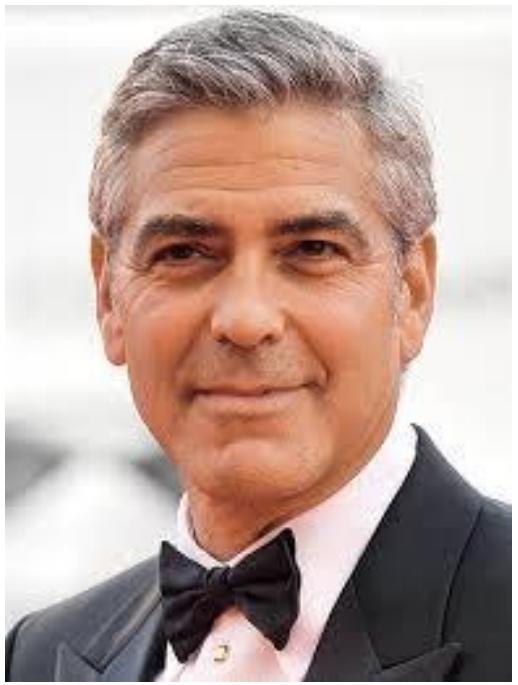
Quais são os objetivos no tratamento da LMC?

Segurança

Efetividade

Custo

Se juntar tudo.....


Como escolher o melhor objetivo ?

“Nesse caso tanto faz”

Pacientes e Médicos tem objetivos diferentes

CHRONIC MYELOID LEUKEMIA SURVEY ON UNMET NEEDS (CML SUN): BALANCING TOLERABILITY AND EFFICACY GOALS OF PATIENTS AND PHYSICIANS THROUGH SHARED TREATMENT DECISION-MAKING

Dr. Fabian Lang

Author(s): Fabian Lang, Zack PEMBERTON-WHITELEY, Joannie Clements, Cristina Ruiz, Delphine Rea, Lisa Machado, Naoto Takahashi, Sung-Ho Moon, Andrew P Grigg, Cornelia Borowczak, Peter Schuld, Pauline Frank, Cristina Constantinescu, Carla Boquimpani, Jorge Cortes

CML SUN - 361 patients and 198 physicians in practice for between three and 35 years, who were personally responsible for treatment decisions for patients with CML

Poster EHA, 2023 - Frankfurt

Figure. Top 5 Tx goals for patients and HCPs by line of therapy[a]

Poster EHA, 2023 - Frankfurt

Objetivo: Sobrevida global igual da população geral

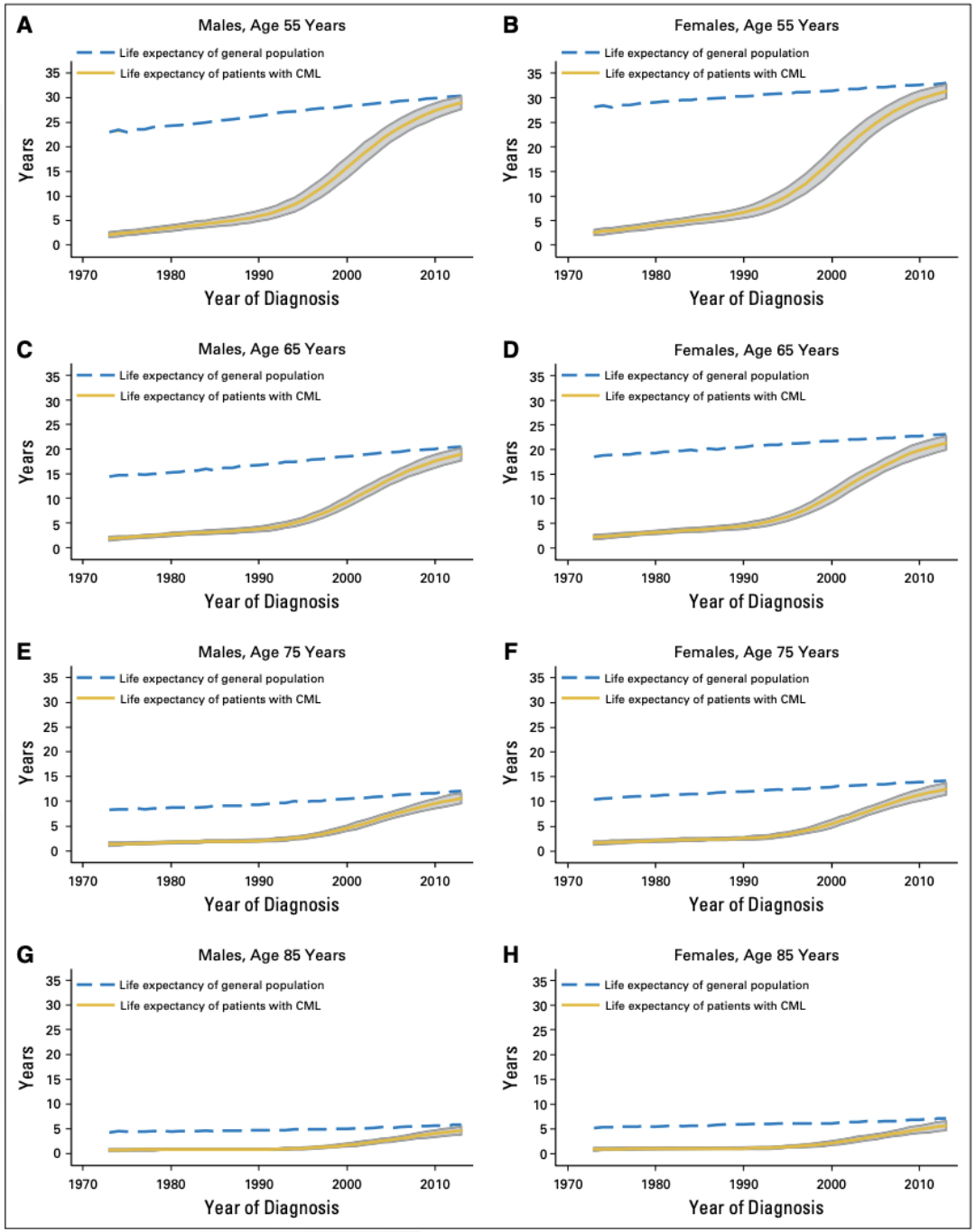
JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

Life Expectancy of Patients With Chronic Myeloid Leukemia Approaches the Life Expectancy of the General Population

Hannah Bower, Magnus Björkholm, Paul W. Dickman, Martin Höglund, Paul C. Lambert, and Therese M.-L. Andersson

Bower, J Clin Oncol 2016 Aug 20;34(24):2851-7



- A expectativa de vida do brasileiro é de 76 anos em média pelos dados do IBGE de 2023.
- A mediana de idade ao diagnóstico do paciente com LMC é de 55 a 60 anos, e no Brasil é de 48 a 50 anos
- Um paciente pode viver em tratamento para a **LMC durante 26 a 28 anos aproximadamente**

Como será tratar um paciente com LMC por 28 anos?

Diagnóstico → 28 anos depois

Nenhuma comorbidade

Objetivo: escolha baseada nas comorbidades

Suggestions for TKI selection for frontline therapy based on selected comorbidities

Comorbidity	Preferred	Less preferred
Diabetes	Imatinib, dasatinib, bosutinib	Nilotinib
Pulmonary disease/pulmonary arterial hypertension	Imatinib, bosutinib, nilotinib	Dasatinib
Gastrointestinal issues	Nilotinib, dasatinib	Imatinib, bosutinib
Cardiovascular	Imatinib, bosutinib	Nilotinib, dasatinib
Peripheral arterial	Imatinib, bosutinib (dasatinib?)	Nilotinib
Liver	Imatinib, dasatinib (nilotinib?)	Bosutinib
Renal	Nilotinib, dasatinib	Imatinib, bosutinib

Cortes, Hematology 2020

Comorbidities		Imatinib	Nilotinib	Dasatinib	Bosutinib	Ponatinib	Asciminib
Cardiovascular	Hypertension						
	Ischemic heart disease						
	Occlusive peripheral artery disease						
	Congestive heart failure						
	Diabetes						
	QT prolongation						
Pulmonary	Pulmonary disease						
	Pulmonary arterial hypertension						
Gastrointestinal issues							
Pancreatic dysfunction							
Liver dysfunction							
Kidney dysfunction							

Legend	
	Risk of related AEs based on comorbidity
Preferred	Very low
	Low
Less preferred	Intermediate
Avoid, if possible	High

Objetivo: escolha baseada nos eventos adversos

	Imatinib	Dasatinib	Nilotinib	Bosutinib	Ponatinib	Asciminib
Hematological						
Neutropenia	++	++	+	+	++	+
Thrombocytopenia	+	++	+	++	++	++
Anemia	+	+	+	+	++	+
Nonhematological						
Edema	+++	–	–	+	–	+
Nausea	++	+	+	+++	+	+
Vomiting	++	+	+	++	+	+
Muscle spasms	+++	–	–	–	–	–
Rash	+	–	+++	+	+++	–
Pleural effusion	–	+++	–	+	–	–
Headache	–	–	+	+	+++	+
Diarrhea	+	+	–	+++	+	–
Fatigue	+	+	+	+	++	+
Liver dysfunction	+	++	+++	+++	+	–
Arterial occlusive events	-	+	++	-	+++	?

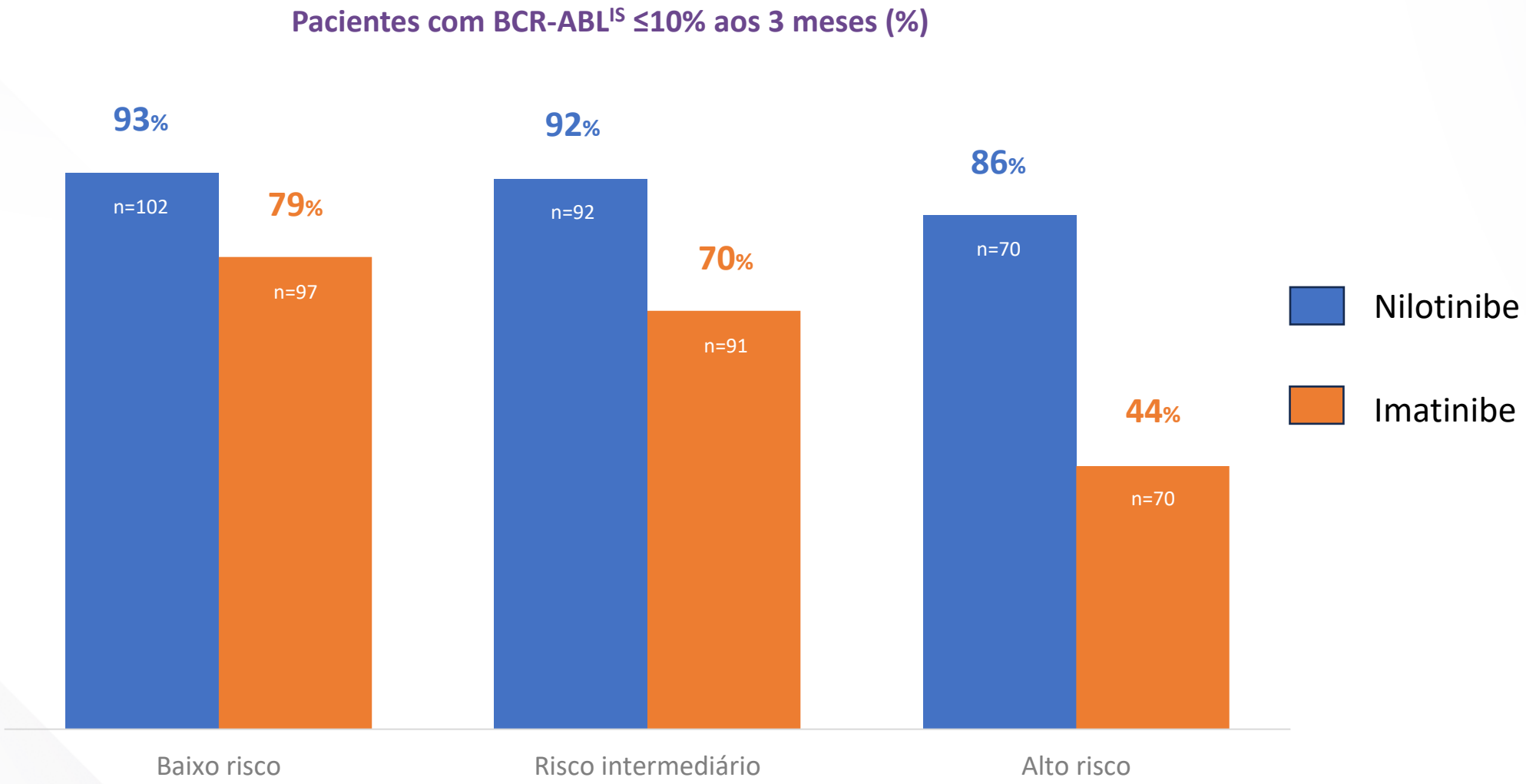
Yoshifuji and Sasaki, Frontiers in Oncology, 2022

Redução de dose do TKI reduz evento adverso

- Imatinibe – Dose 400 mg para 300mg em RMP = Melhor tolerância sem perda da eficácia
- Dasatinibe – Dose de 50mg/dia pode prevenir a incidência de derrame pleural e hipertensão arterial
- Nilotinibe - No estudo NILO-RED, o Nilotinibe foi reduzido para apenas uma vez ao dia após os pacientes atingirem MMR.
- Bosutinibe - Dose mais baixa de bosutinibe 400 ou 300mg pode ser considerada em pacientes frágeis, pacientes com comorbidades graves que falharam em múltiplos TKI
- Ponatinibe – Estudo Optic evidenciou melhor resposta e menos EA nos pacientes que iniciaram com 45mg e reduziram para 15mg após alcançarem PCR <1%

Cervantes, Ann Hematol (2017) 96(1):81–5
Murai, Lancet Haematol (2021) 8(12):e902–e11
Rea, Blood (2017) 130(Supplement 1):318
Latagliata, Blood (2019) 134(Supplement_1):1649
Cortes, Blood (2021) 138(21):2042–50

Objetivo: Escolha do TKI baseado no risco prognóstico



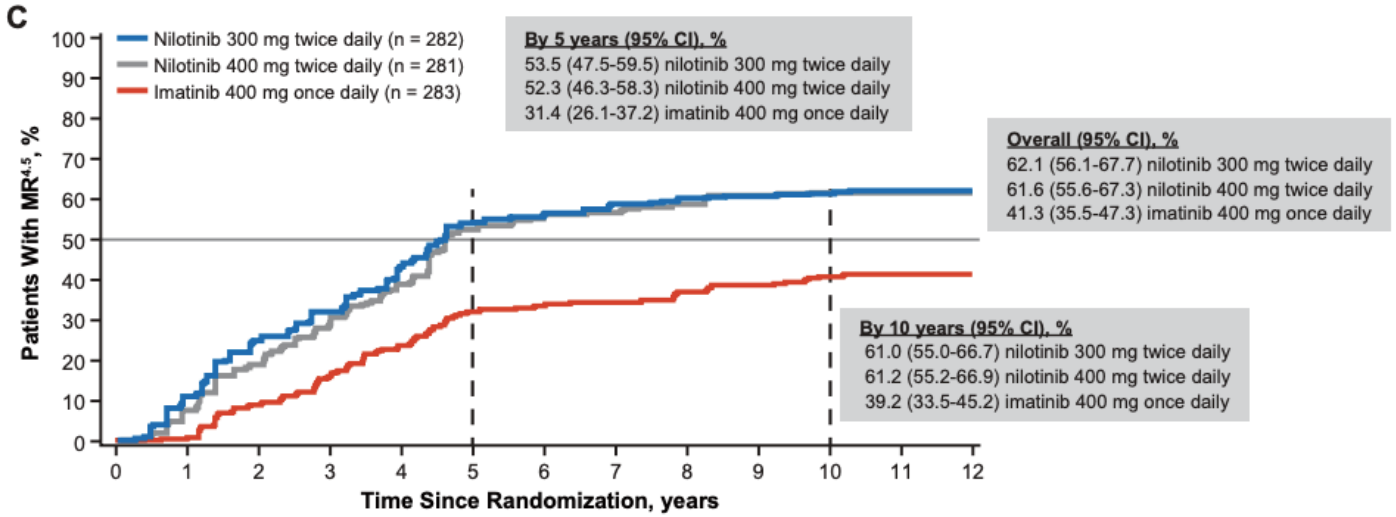
Hochhaus A, et al. Leukemia. 2016;30(5):1044-54.

Remember to use ELTS to avoid labelling many as high-risk

(b) Risk strata proportions and outcome

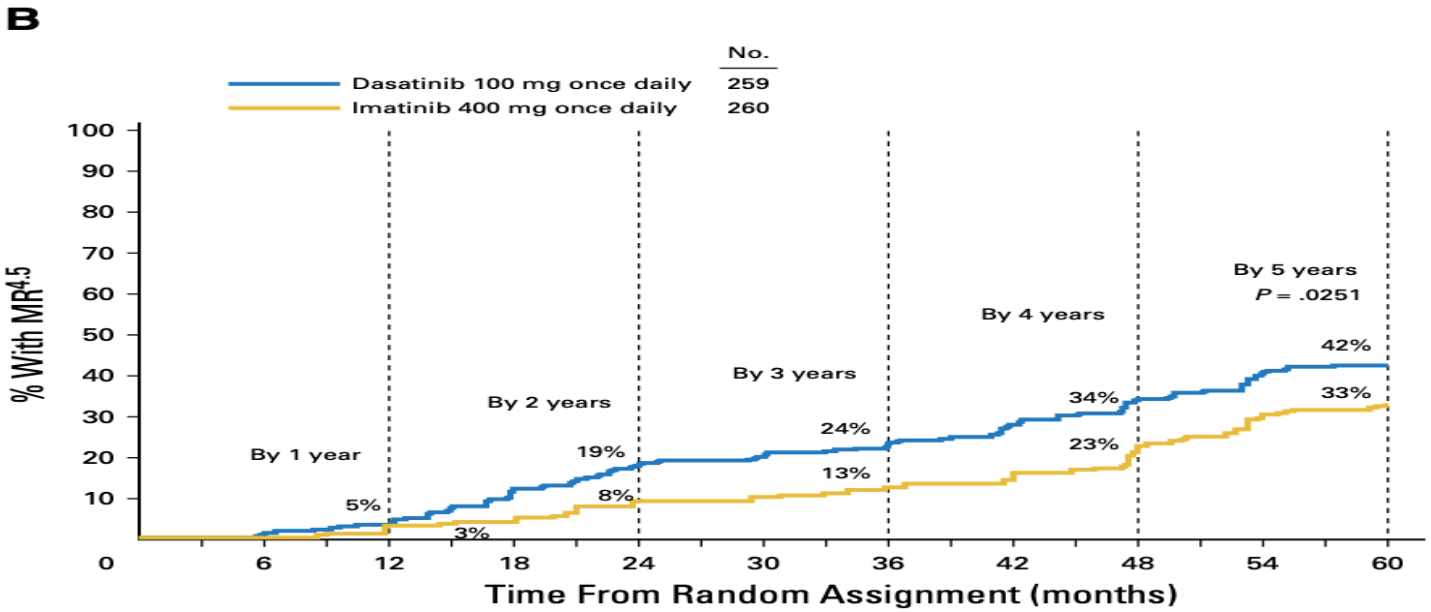
	Low risk		Intermediate risk		High risk	
$n = 5154$	Sokal	ELTS	Sokal	ELTS	Sokal	ELTS
%	38	55	38	28	23	13
10-year OS	89%	88%	81%	79%	75%	68%
6-year LRD	3%	2%	4%	5%	8%	12%

Objetivo: Escolha baseada na intenção de TFR



ENESTnd

Nilotinibe x Imatinibe



DASISION

Dasatinibe x Imatinibe

Escolha baseada na personalização

- Se paciente de baixo/intermediário risco prognóstico ➔ Imatinibe
- Se paciente de alto risco prognóstico sem comorbidades ➔ TKI 2G
- Se paciente de alto risco prognóstico com comorbidades ➔ Imatinibe
- Se paciente jovem com intenção de interromper (exemplo: gestação programada) ➔ TKI 2G
- Se paciente com insuficiência renal ➔ TKI 2G
- Se paciente idoso com ou sem comorbidades mesmo em risco alto ➔ Imatinibe

Perspectivas Futuras

The NEW ENGLAND JOURNAL of MEDICINE

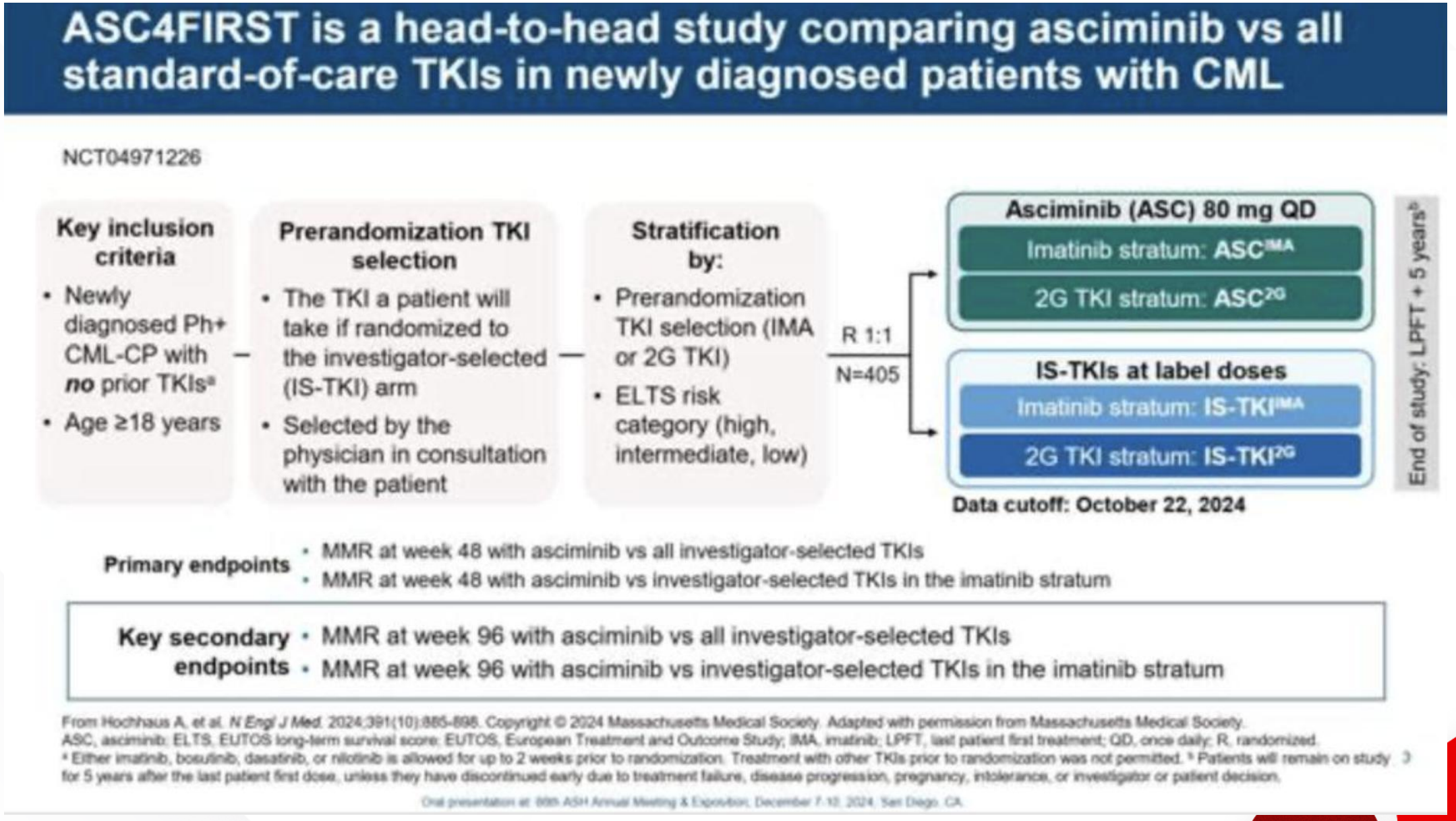
ORIGINAL ARTICLE

Asciminib in Newly Diagnosed Chronic Myeloid Leukemia

Authors: Andreas Hochhaus, Dr.Med., Jianxiang Wang, M.D., Dong-Wook Kim, M.D., Ph.D., Dennis Dong Hwan Kim, M.D., Ph.D., Jiri Mayer, M.D., Yeow-Tee Goh, M.B., B.S., M.Med., Philipp le Coutre, M.D., +15 , for the ASC4FIRST Investigators* Author Info & Affiliations

Published May 31, 2024 | N Engl J Med 2024;391:885-898 | DOI: 10.1056/NEJMoa2400858 | VOL. 391 NO. 10

Perspectivas Futuras



From Hochhaus A, et al. *N Engl J Med*. 2024;391(10):885-898. Copyright © 2024 Massachusetts Medical Society. Adapted with permission from Massachusetts Medical Society.
ASC, asciminib; ELTS, EUTOS long-term survival score; EUTOS, European Treatment and Outcome Study; IMA, imatinib; LPFT, last patient first treatment; QD, once daily; R, randomized.
[a] Either imatinib, bosutinib, dasatinib, or nilotinib is allowed for up to 2 weeks prior to randomization. Treatment with other TKIs prior to randomization was not permitted. [b] Patients will remain on study for 5 years after the last patient first dose, unless they have discontinued early due to treatment failure, disease progression, pregnancy, intolerance, or investigator or patient decision.

Oral presentation at: 66th ASH Annual Meeting & Exposition; December 7-10, 2024; San Diego, CA.


OBRIGADA