Novartis ASCO Investor Event

Chicago, June 2, 2024

NOVARTIS | Reimagining Medicine

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EVP, Chief Commercial
Officer - US

Agenda

1   **Novartis legacy in CML and current unmet needs**

2   *Scemblix®* ASC4FIRST results

3   *Scemblix®:* Establishing the 1L CML treatment of choice

4   Q&A

Novartis has a 20+ year legacy of innovation in CML, transforming a once deadly disease into a chronic condition

Novartis legacy in CML

2001

Introduction of **first targeted therapy** improves survival for CML patients

gleevec®
(imatinib mesylate) tablets
100mg, 400mg

2007

Continued focus on **deeper levels of response** and disease control: MMR → DMR → **TFR**

Tasigna®
(nilotinib) 150mg, 200mg capsules

Today

Goal of **transforming SoC once again** by potentially enabling more patients to meet treatment goals with better tolerability

SCEMBLIX®
(asciminib) 20mg, 40mg tablets

CML is now a chronic cancer

~17k newly diagnosed patients/year

10-year survival rate of ~95%

Most patients have a life expectancy comparable to the general population

Vast majority take daily TKI therapy for the rest of their lives

CML – Chronic myeloid leukemia. For all following usage in this presentation, CML represents Philadelphia positive chronic phase CML (Ph+ CML-CP)   TKI – Tyrosine kinase inhibitor.   MMR – Major molecular response.   DMR – Deep molecular response.   TFR – Treatment-free remission.   SoC – Standard of care.

However, treatments that optimize efficacy and safety are still needed

Inadequate control of CML and TKI-related AEs can increase risk of progression

~40% of 1L CML patients **need to change therapy by 5 years** due to either resistance, intolerance and treatment related complications[1-4] ; ~30% of patients switch within the first year of their second therapy[5]

~50% of patients **do not achieve DMR even after 4 years** of switching from their first treatment[6]

~25% of treated CML patients manage to achieve **TFR,** with some requiring ~8 years to qualify for TFR[7]

Long-term use of 2G TKIs is associated with **AEs such as pleural effusion, GI and CV events** due to off-target effects[8,10]

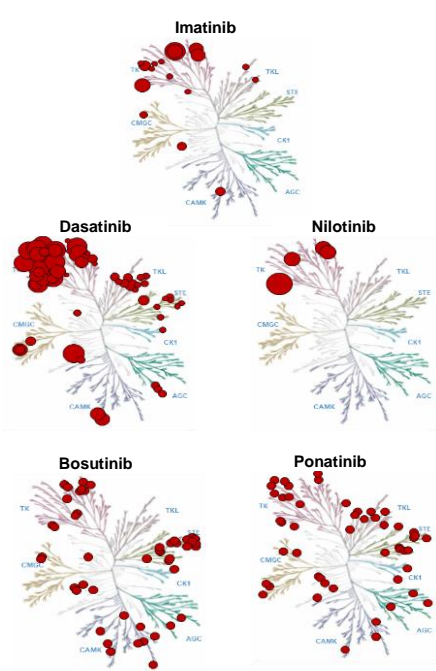Persistent AEs remain the **most common reason for intentional non-adherence** to TKI treatment[9]

Novel treatments with differentiated mechanism of action may allow patients to stay on therapy longer and better achieve treatment goals

TKI – Tyrosine kinase inhibitor.   MMR – Major molecular response.   DMR – Deep molecular response (MR4, MR4.5 etc., where MR4 represents at least a 4-log reduction i.e., BCR-ABL 1IS ≤0.01%).   TFR – Treatment-free remission.   AE – Adverse event.   GI – Gastrointestinal.   CV – Cardiovascular.   Please refer to the appendix for references 1-9.   10. 2G TKIs refer to second generation TKIs which are nilotinib, dasatinib, and bosutinib
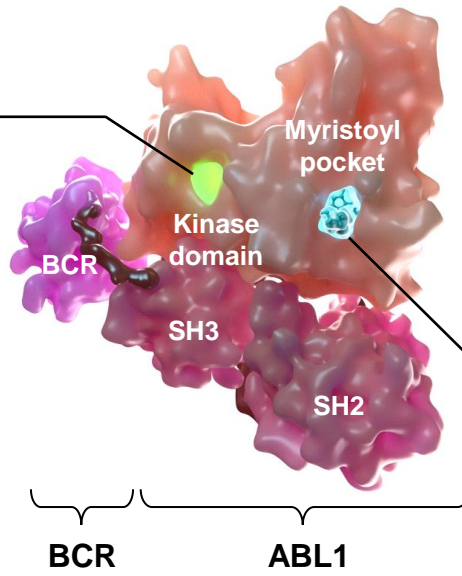
Scemblix was designed for enhanced efficacy and minimized off-target activity vs current standard-of-care TKIs[4]
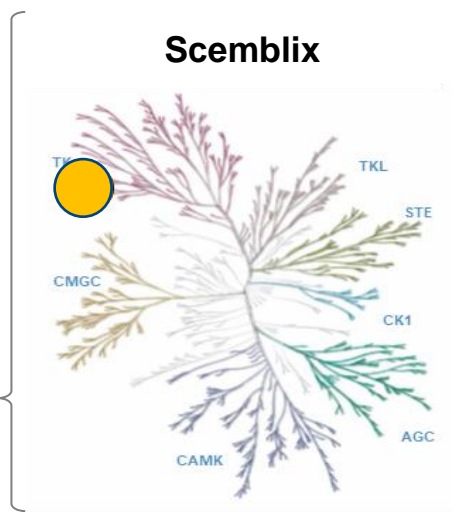
ATP-competitive TKIs[1,4]

Scemblix: 1st BCR::ABL1 inhibitor specifically targeting ABL myristoyl pocket[2,3,4]

Imatinib

Dasatinib   **Nilotinib**

Bosutinib   **Ponatinib**

ATP-binding site[1]

Myristoyl pocket

Kinase domain

BCR

SH3

SH2

BCR   ABL1

Scemblix binding site

Scemblix

● Kinases bound by ATP-competitive TKIs[1]

● Kinases bound by STAMP inhibitors[2]

ATP – adenosine triphosphate.   CAMK – calcium/calmodulin-dependent protein kinases; CK1, cell kinase.   STAMP – Specifically Targeting the ABL Myristoyl Pocket. STE, serine/threonine kinases.   TKL – tyrosine kinase-like.
1. Each ATP-competitive TKIs inhibit multiple kinases due to similarities between ATP binding pockets.   2. Myristoyl binding site unique for ABL-1 protein.   3. BCR-ABL1 fusion protein kinase activity leads to uncontrolled growth of myeloid cells.   4. Please refer to the appendix for references.

In the Ph3 ASCEMBL study, Scemblix more than doubled MMR rate vs bosutinib with a favorable safety profile in 3L+ CML...

Efficacy[1]

- **Scemblix is the 1st agent to show superiority vs 2G TKI**, more than doubling the MMR rate vs bosutinib

Major Molecular Response (MMR) Rates at week 96

Bar chart — Patients, %:
- Scemblix (n=156): 37.6
- Bosutinib (n=76): 15.8
- Difference: 21.7%
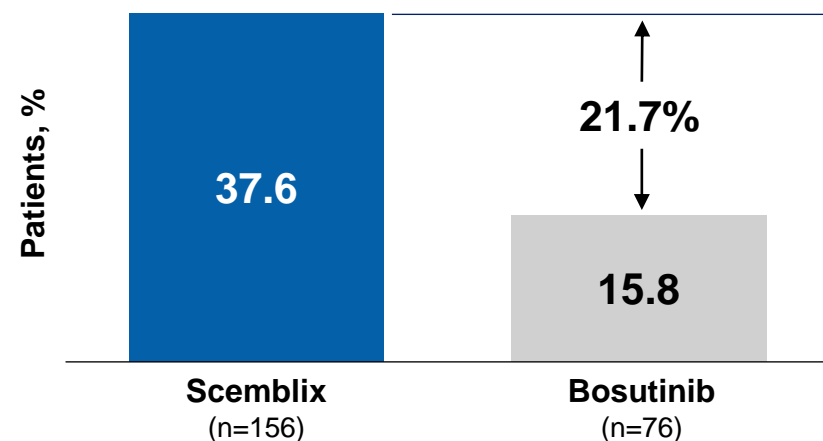
Safety and tolerability[1,2]

- AEs leading to treatment discontinuation were **~4x lower** with Scemblix vs bosutinib
- Median **duration of exposure** was over **3x longer**
- Scemblix showed **improvements in symptoms and health-related QoL**[2]

Durability[3,4]

- **Sustained efficacy and safety** with **~4 years** median follow-up in **ASCEMBL**[3]
- **Up to 8 years** of follow-up in **X2101 FIH study**[4]

1. ASCEMBL Ph3 week 96: Hochhaus A. et al., Leukemia 2023; 37:617–626.   2. Rea D et al., Leukemia 2023;37:1060-1067.   3. ASCEMBL Ph3 end of study: Mauro MJ et al., ASH2023, poster 4536.
4. X2101 FIH final results: Hochhaus A. et al., ASH2023, oral presentation 450.

...which has led to rapid uptake in clinical practice, and the opportunity to study Scemblix in earlier lines of treatment

Scemblix uptake in 3L+ CML

>70 approvals around the world[1]

Conversion of accelerated approval to full approval in US[2]

Included in NCCN guidelines[3]

Leading share in both new starts and total TRx in 3L+[4]

Use across academic centers and the community setting[5]

Switches from all other TKIs[5]

Compelling profile in 3L+ CML presents the opportunity to evaluate Scemblix in earlier lines of treatment

1. Novartis internal data on file.   2. Scemblix Label FDA dated October 12th 2022 --- Efficacy-Labeling Change With Clinical Data-- from conditional to full approval.
3. Shah NP et al., Journal of the National Comprehensive Cancer Network 2024, 22(1), 43-69.   4. IQVIA Market Sizing Report, 2024.   5. Atallah et al., Blood 2023; 142 (Supplement 1):1809.

Agenda

1   Novartis legacy in CML and current unmet needs
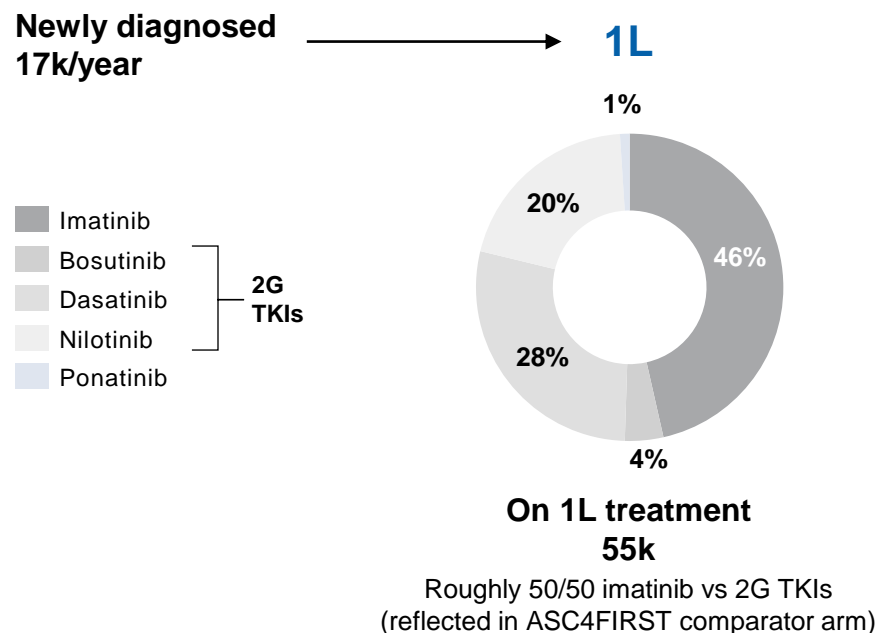
2   ***Scemblix* ASC4FIRST results**

3   *Scemblix:* Establishing the 1L CML treatment of choice

4   Q&A

Many newly diagnosed CML patients still do not reach efficacy goals with current standard-of-care TKIs

1L CML treatment landscape[1,2,3]

Newly diagnosed 17k/year → **1L**

Legend:
- Imatinib
- Bosutinib ⎤
- Dasatinib ⎬ **2G TKIs**
- Nilotinib ⎦
- Ponatinib

Donut chart:
- 1%
- 46%
- 20%
- 28%
- 4%

On 1L treatment 55k

Roughly 50/50 imatinib vs 2G TKIs
(reflected in ASC4FIRST comparator arm)

Remaining unmet need in 1L CML

~25% of 1L patients **switch treatments in the 1st year**[4]

~50% of 1L patients **do not meet efficacy goals** (MMR) at 1 year; even fewer achieve deep responses by 2 years[5-7]
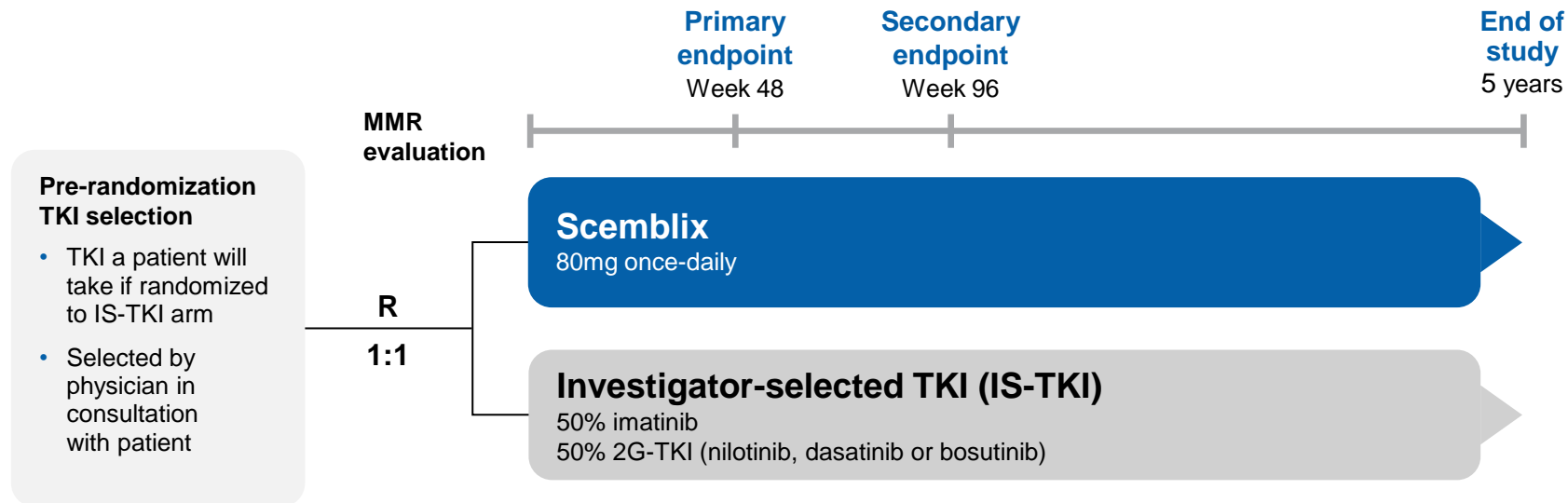
⚠ Persistent AEs (such as diarrhea, edema, rash) remain the **most common reason for intentional non-adherence** to TKI treatment[8]

Faster and deeper molecular response with favorable safety and tolerability remains the key unmet need for newly diagnose patients with CML

MMR – Major molecular response (BCR-ABL 1IS ≤0.1%).   1. Newly diagnosed: Kantar health CML incidence in G7 (US, EU5, JP), patients in 2024.   2. CML prevalence in G7, 2024: Kantar health.   3. IQVIA Market Sizing, IPSOS & IQVIA Oncology Dynamics (G7, MAT Jun 2023).   Please refer to appendix for references 4-8

The Ph3 ASC4FIRST study was designed to reflect current clinical practice and unmet needs in newly diagnosed CML patients

ASC4FIRST: Adult patients with newly diagnosed Ph+ CML-CP with no prior TKIs (n=405)

Primary endpoint — Week 48
Secondary endpoint — Week 96
End of study — 5 years

MMR evaluation

Pre-randomization TKI selection
- TKI a patient will take if randomized to IS-TKI arm
- Selected by physician in consultation with patient

R 1:1

Scemblix 80mg once-daily

Investigator-selected TKI (IS-TKI)
50% imatinib
50% 2G-TKI (nilotinib, dasatinib or bosutinib)

Primary endpoints:
- MMR week 48 vs all IS-TKIs
- MMR at week 48 vs imatinib

Key secondary endpoints:
- MMR at week 96 vs all IS-TKIs
- MMR at week 96 vs imatinib

Other endpoints include:
- MMR vs 2G TKIs
- DMR (MR4/MR4.5)
- Type, frequency and severity of AEs including discontinuation due to AEs
- Change in QoL

Stratification: **Pre-randomization TKI selection** Imatinib or 2G-TKI   **ELTS** High/intermediate/low

Ph+ CML-CP – Philadelphia positive chronic myeloid leukemia in chronic phase.   MMR – Major molecular response (BCR-ABL 1IS ≤0.1%).   DMR – Deep molecular response (MR4, MR4.5, MR5).   MR4 – at least a 4-log reduction i.e., BCR-ABL 1IS ≤0.01%.   MR4.5 – at least a 4.5 log reduction i.e., BCR-ABL 1IS ≤0.0032%.   MR5 – at least a 4 log reduction i.e., BCR-ABL 1IS ≤0.001%   TKI – Tyrosine kinase inhibitor.   IS – Investigator-selected.   ELTS - EUTOS long-term survival score.   ASC – asciminib.   QoL – Quality of life.
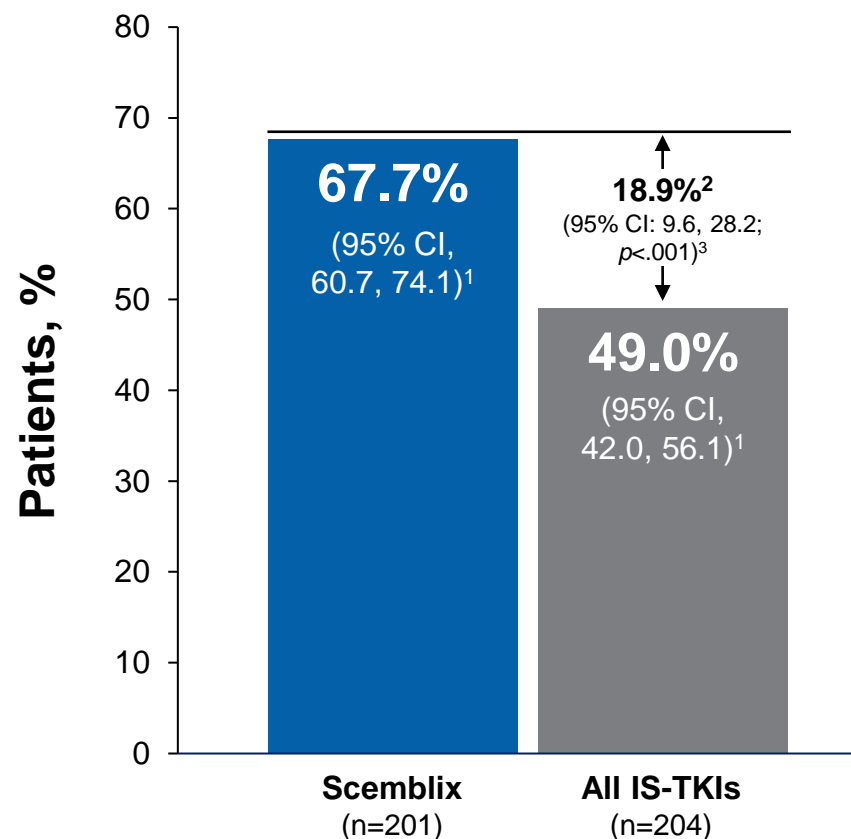
Baseline characteristics were similar between the arms and representative of the CML population

Variable	Scemblix		IS-TKI	
	Imatinib stratum (n=101)	2G TKI[1] stratum (n=100)	Imatinib stratum (n=102)	2G TKI[1] stratum (n=102)
Median age (range), years	56.0 (21.0-79.0)	43.0 (18.0-76.0)	54.5 (20.0-86.0)	43.0 (19.0-83.0)
Age group, %				
18 to <65 years	68.3	86.0	68.6	83.3
65 to <75 years	**23.8**	12.0	**21.6**	11.8
≥75 years	**7.9**	2.0	**9.8**	4.9
Male, %	61.4	69.0	63.7	58.8
Framingham estimated 10-year cardiovascular disease risk categories, %				
Low risk (<10%)	40.6	68.0	39.2	70.6
Intermediate risk (10%–20%)	**20.8**	11.0	**28.4**	14.7
High risk (≥20%)	**38.6**	21.0	**32.4**	14.7
ELTS, %				
Low	61.4	60.0	62.7	59.8
Intermediate	29.7	26.0	29.4	26.5
High	8.9	14.0	7.8	13.7

Patients pre-selected to receive imatinib ("imatinib stratum") had more patients >65 years old and more patients with higher CV disease risk than those pre-selected to receive 2G TKI[1] ("2G TKI[1] stratum")
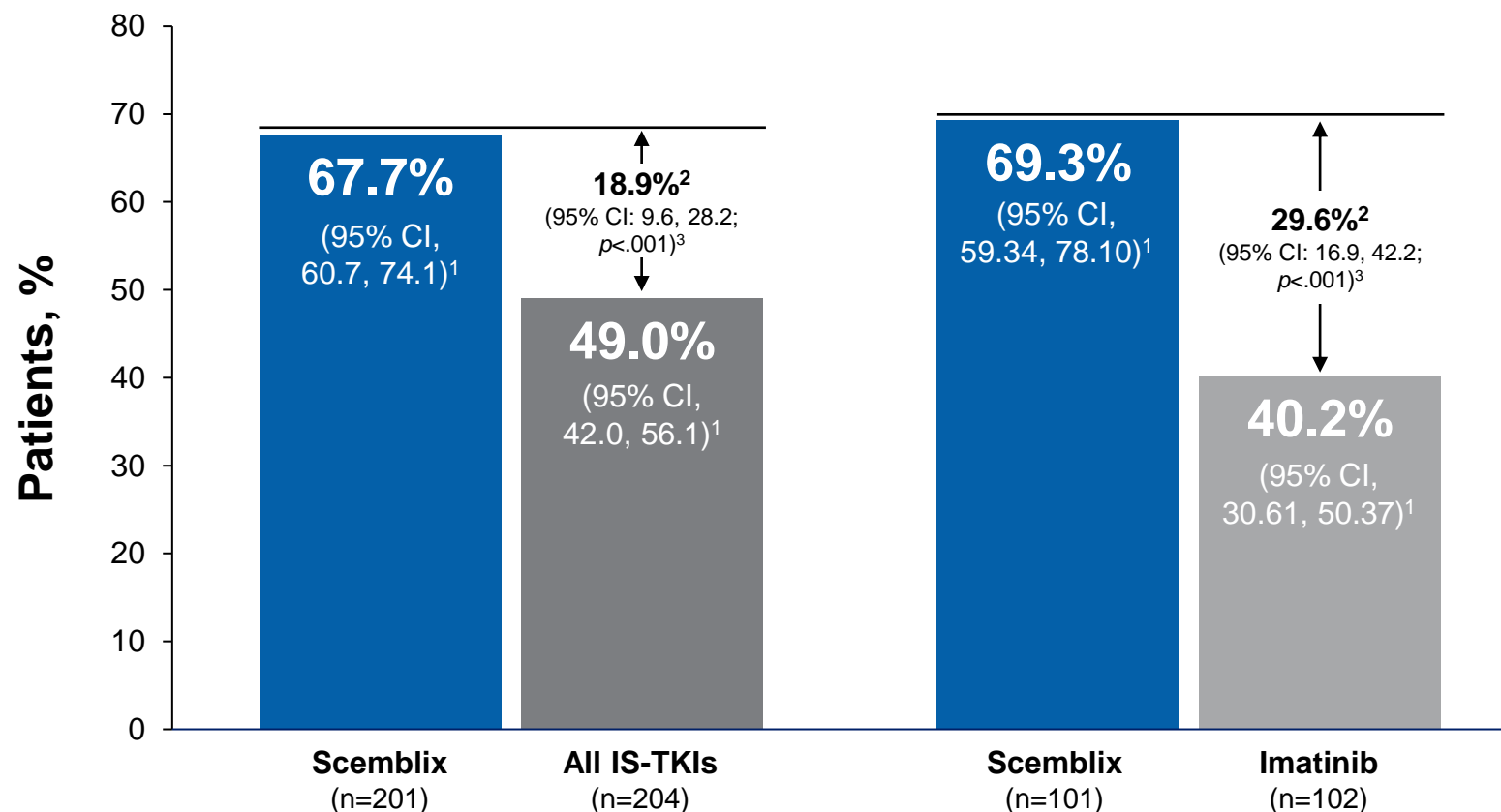
Scemblix demonstrated clinically meaningful and statistically significant MMR benefit of nearly 20% vs investigator-selected TKIs (IS-TKIs)

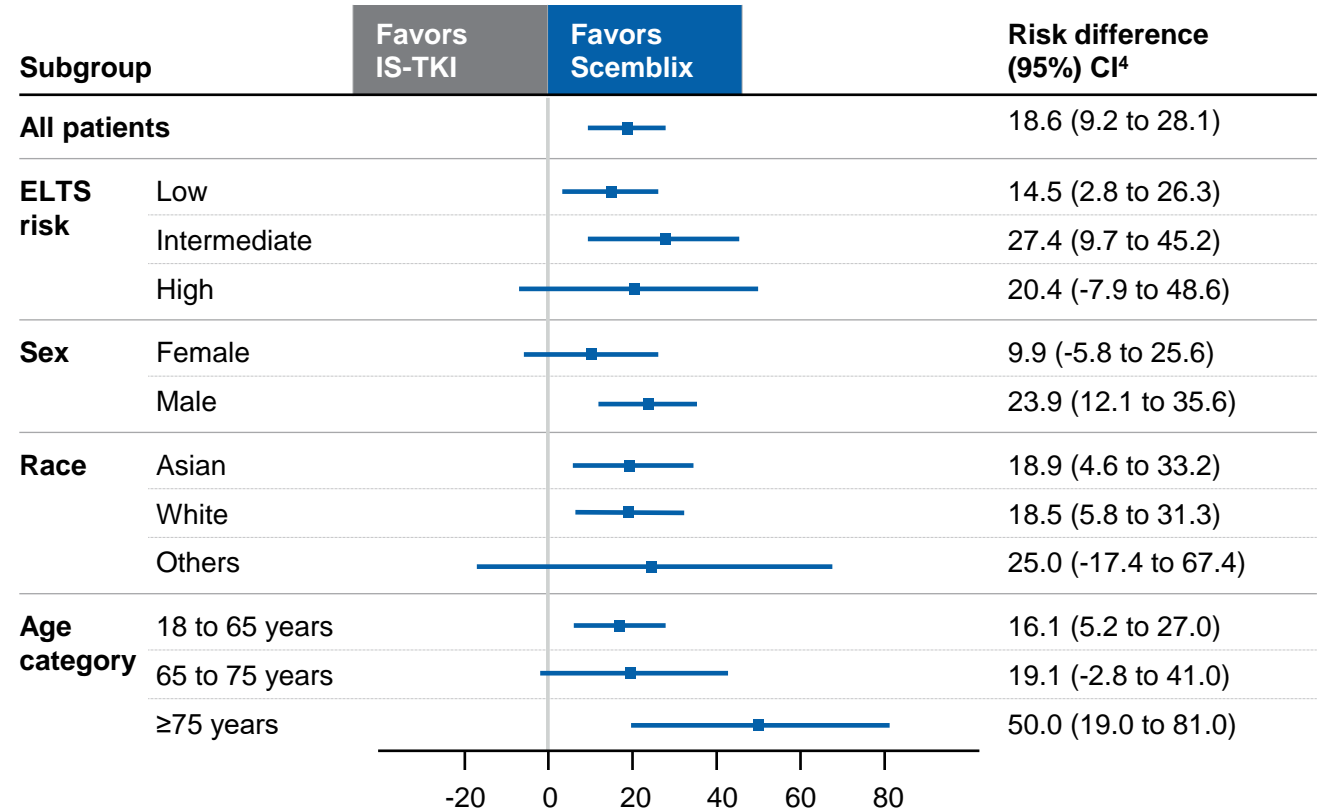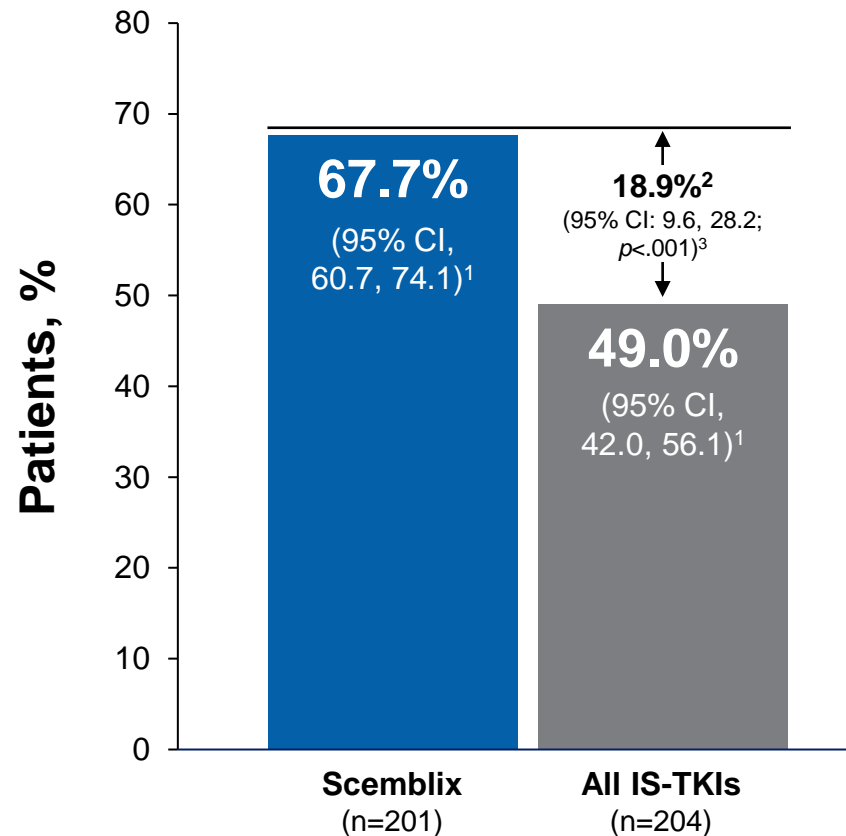Patients, %

67.7%
(95% CI,
60.7, 74.1)[1]

18.9%[2]
(95% CI: 9.6, 28.2;
p<.001)[3]

49.0%
(95% CI,
42.0, 56.1)[1]

Scemblix
(n=201)

All IS-TKIs
(n=204)

MMR rate at week 48 was superior vs all IS-TKIs and vs imatinib, meeting both primary endpoints with high statistical significance

Patients, %

	Scemblix (n=201)	All IS-TKIs (n=204)	Scemblix (n=101)	Imatinib (n=102)
MMR rate	67.7% (95% CI, 60.7, 74.1)[1]	49.0% (95% CI, 42.0, 56.1)[1]	69.3% (95% CI, 59.34, 78.10)[1]	40.2% (95% CI, 30.61, 50.37)[1]

Difference Scemblix vs All IS-TKIs: **18.9%**[2] (95% CI: 9.6, 28.2; *p*<.001)[3]

Difference Scemblix vs Imatinib: **29.6%**[2] (95% CI: 16.9, 42.2; *p*<.001)[3]

Higher MMR rates were consistent across all demographic and prognostic subgroups

Patients, %

- Scemblix (n=201): **67.7%** (95% CI, 60.7, 74.1)[1]
- All IS-TKIs (n=204): **49.0%** (95% CI, 42.0, 56.1)[1]
- **18.9%**[2] (95% CI: 9.6, 28.2; *p*<.001)[3]

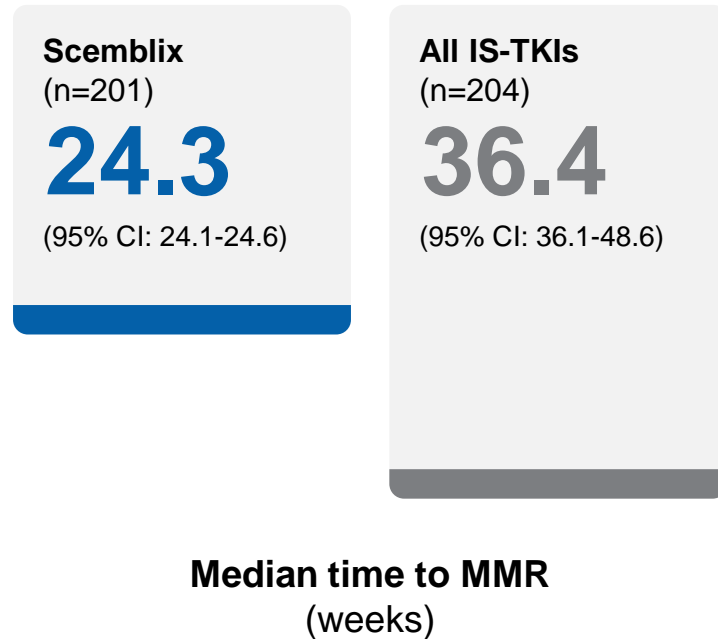| Subgroup		Favors IS-TKI ←	→ Favors Scemblix	Risk difference (95%) CI[4]
All patients				18.6 (9.2 to 28.1)
ELTS risk	Low			14.5 (2.8 to 26.3)
	Intermediate			27.4 (9.7 to 45.2)
	High			20.4 (-7.9 to 48.6)
Sex	Female			9.9 (-5.8 to 25.6)
	Male			23.9 (12.1 to 35.6)
Race	Asian			18.9 (4.6 to 33.2)
	White			18.5 (5.8 to 31.3)
	Others			25.0 (-17.4 to 67.4)
Age category	18 to 65 years			16.1 (5.2 to 27.0)
	65 to 75 years			19.1 (-2.8 to 41.0)
	≥75 years			50.0 (19.0 to 81.0)

x-axis: -20, 0, 20, 40, 60, 80

Hughes TP et al., 2024 ASCO Annual Meeting LBA6500. IS-TKIs – Investigator selected TKIs. CI – Confidence interval. CMH – Cochran-Mantel-Haenszel. NA – Not applicable. 1. Clopper-Pearson 95% CI. 2. The common risk difference and its 95% CI estimated using the Mantel-Haenszel method after stratifying for (a) pre-randomization selected TKI, and (b) baseline ELTS risk groups (both IRT data). 3. Adjusted 1-sided p-value calculated based on the graphical gatekeeping procedure. The null hypothesis is rejected if the adjusted p-value ≤0.025. 4. Unstratified risk difference.
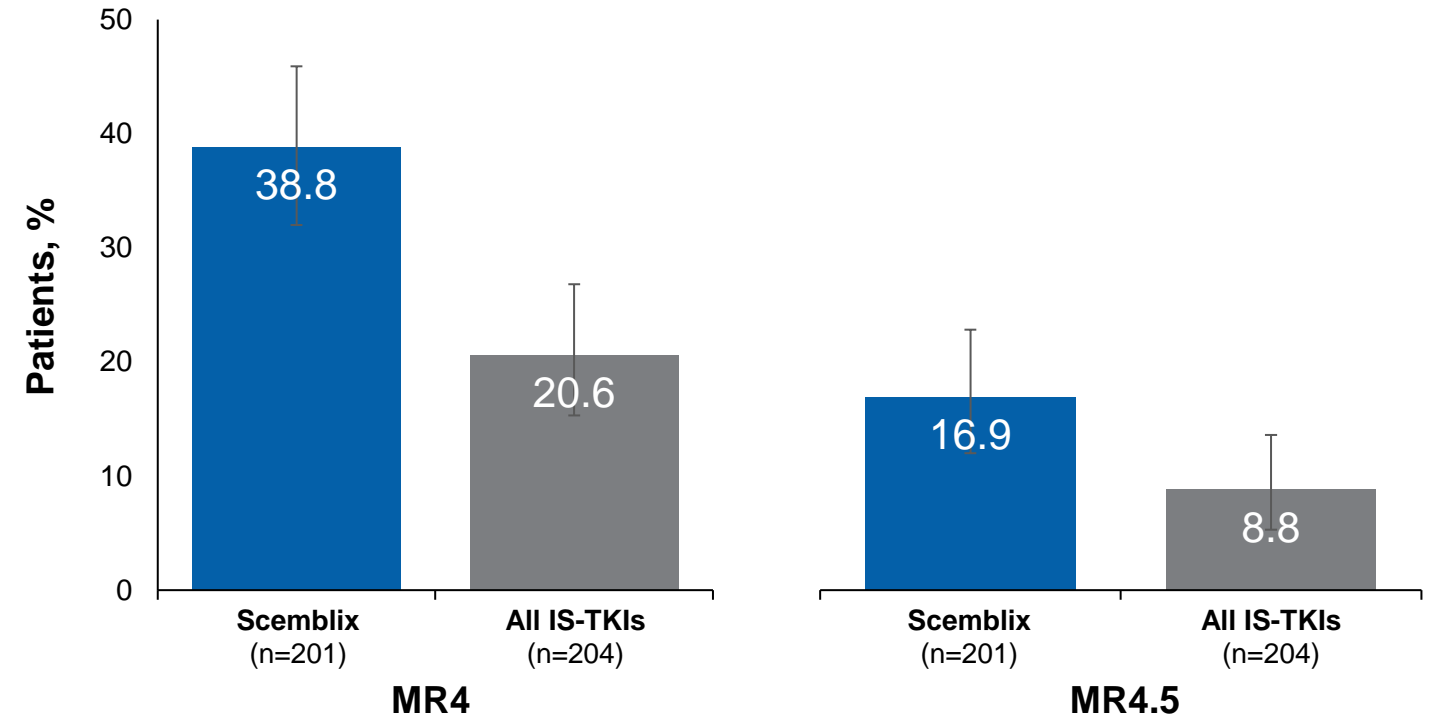
Scemblix patients also achieved earlier and deeper molecular responses vs all IS-TKIs...
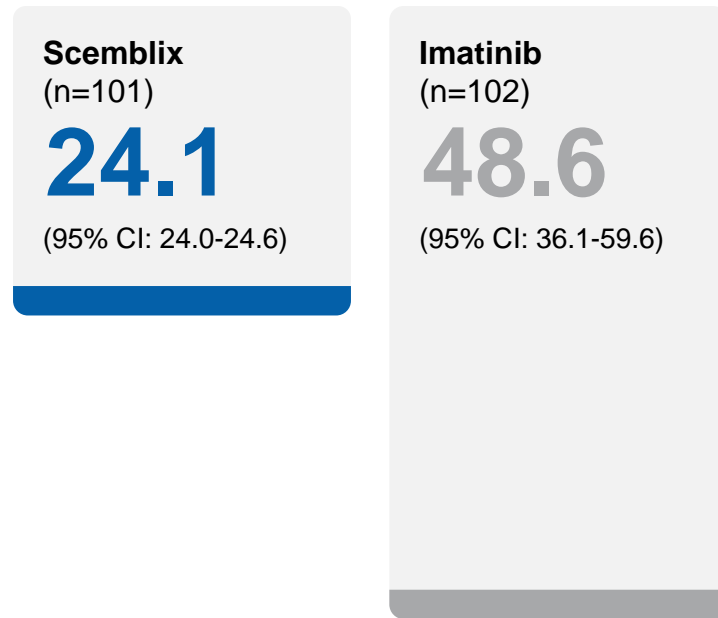
Reduced Time to MMR by 1/3

Scemblix
(n=201)

24.3

(95% CI: 24.1-24.6)

All IS-TKIs
(n=204)

36.4

(95% CI: 36.1-48.6)

Median time to MMR
(weeks)

Nearly doubled deep molecular responses at 1 year

... as well as earlier and deeper molecular responses vs imatinib

Median Time to MMR
(weeks)

Scemblix
(n=101)

24.1

(95% CI: 24.0-24.6)

Imatinib
(n=102)

48.6

(95% CI: 36.1-59.6)

MR4

Patients, %

	Scemblix (n=101)	Imatinib (n=102)
	42.6	17.8

MR4.5

	Scemblix (n=101)	Imatinib (n=102)
	17.8	4.9

Compared to 2G TKIs[4], Scemblix showed numerically higher MMR rates, earlier achievement of MMR, and deeper responses

MMR
(not powered)

Patients, %

Scemblix: 66.0% (95% CI, 55.9, 75.2)[1]

2G TKIs: 57.8% (95% CI, 47.7, 67.5)[1]

8.2%[2] (95% CI: -5.1, 21.5)

Scemblix (n=100)

2G TKIs[5] (n=102)

Median Time to MMR
(weeks)

Scemblix (n=100)
24.3
(95% CI: 24.1-35.6)

2G TKIs[4] (n=102)
36.1
(95% CI: 24.4-48.1)

MR4

Scemblix: 35.0 (n=100)

2G TKIs[5]: 26.5 (n=102)

MR4.5

Scemblix: 16.0 (n=100)

2G TKIs[5]: 12.8 (n=102)

Scemblix showed favorable safety and tolerability vs all IS-TKIs...

Fewer grade ≥3 AEs vs all IS-TKIs
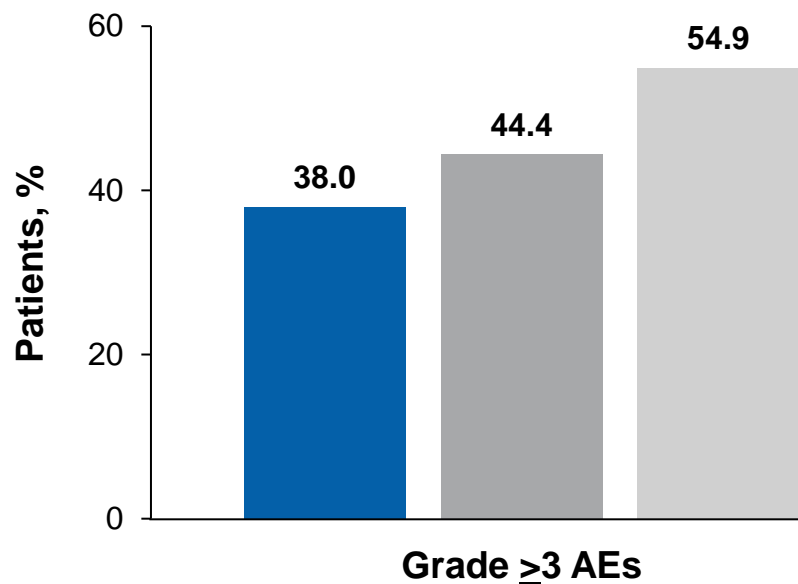
Fewer AEs leading to interruptions/discontinuations

Patients, %

Grade >3 AEs: Scemblix 38.0, Imatinib 44.4, 2G TKIs 54.9

AEs leading to discontinuation: Scemblix 4.5, Imatinib 11.1, 2G TKIs 9.8

AEs leading to dose adjustment/interruption: Scemblix 30.0, Imatinib 39.4, 2G TKIs 52.9
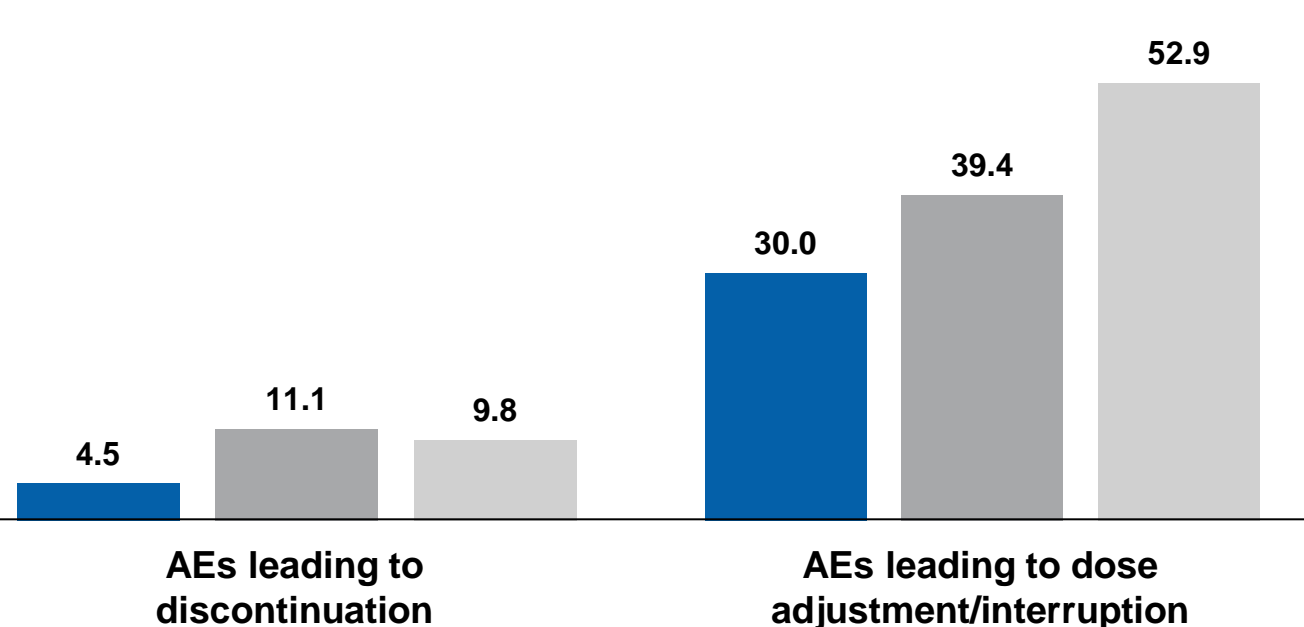
■ Scemblix (n=200)[1] ■ Imatinib (n=99)[1] ■ 2G TKIs[2] (n=102)[1]

... with lower rates of non-hematological AEs impacting patient quality of life

Scemblix (n=200)[1] — All grade / Grade ≥3

Imatinib (n=99)[1] — All grade / Grade ≥3

2G TKIs[2] (n=102)[1] — All grade / Grade ≥3

AE	Scemblix All grade	Scemblix Grade ≥3	Imatinib All grade	Imatinib Grade ≥3	2G TKIs All grade	2G TKIs Grade ≥3
Diarrhea	15.5		25.5	1.0	26.3	
Fatigue	14.0	0.5	17.6		14.1	1.0
Headache	13.5	0.5	21.6		8.1	
Myalgia	13.0	0.5	14.7		17.2	
Rash	13.0		21.6	1.0	10.1	2.0
Lipase increased	11.5	3.0	10.8	3.9	14.1	1.0
Constipation	9.5		12.7	1.0	4.0	
Nausea	9.0		17.6		21.2	
Increased alanine aminotransferase	7.0	2.0	18.6	7.8	6.1	2.0
Upper respiratory tract infection	7.0		7.8		10.1	1.0
Increased blood alkaline phosphatase	5.5		5.9		13.1	
Vomiting	5.5		5.9		12.1	
Increased blood bilirubin	2.5		10.8		2.0	1.0
Increased aspartate aminotransferase	2.0	0.5	14.7	2.9	6.1	1.0
Muscle spasms	2.0		4.9		19.2	
Periorbital/face edema	1.0		20.2	1.0	1.0	

Patients, %

Hughes TP et al., 2024 ASCO Annual Meeting LBA6500.   1. Safety analyses consisted of patients who received ≥1 dose of study drug. Patients were analyzed according to the study treatment received. The most common AEs leading to treatment discontinuation were lipase increases with Scemblix (1.5%), diarrhea and lymphopenia with imatinib (2.0% each), and pleural effusion with 2G TKIs (2.0%).   2. Investigator selected 2G TKIs – nilotinib, dasatinib, bosutinib.

Better benefit-risk profile vs current SoC TKIs positions Scemblix as a potential therapy of choice for newly diagnosed CML patients upon approval

Scemblix demonstrated superior efficacy...

✓ Superior MMR rates vs IS-TKIs and vs imatinib alone

✓ Consistent results regardless of baseline characteristics

✓ Earlier achievement of MMR and greater depth of responses

✓ Improvement vs 2G TKI[1] in MMR rate, speed and depth of responses

...with a favorable safety and tolerability profile

✓ Fewer grade ≥3 AEs

✓ Fewer dose adjustments/interruptions needed to manage AEs

✓ Half the rate of all-grade AEs leading to discontinuation

✓ Lower rates and severity of most AEs associated with 2G TKI[1] class and impacting patient lives

Hughes TP et al., 2024 ASCO Annual Meeting LBA6500.   SoC – Standard of care.   1. Investigator selected 2G TKIs – nilotinib, dasatinib, bosutinib.
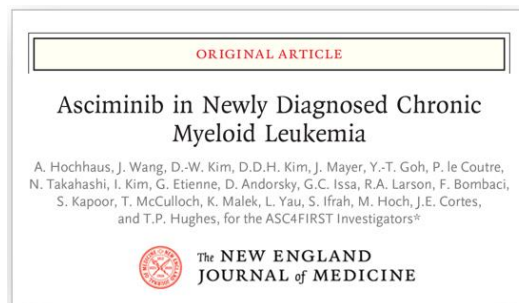
NOVARTIS | Reimagining Medicine

ASC4FIRST data recognized as a major advancement in CML innovation by regulators and the scientific community

FDA Breakthrough designation in 1L CML

Granted based on positive data from ASC4FIRST study

Previously received BTD in patients with 3L+ CML and T315I mutation

NEJM publication[1]

ORIGINAL ARTICLE

Asciminib in Newly Diagnosed Chronic Myeloid Leukemia

A. Hochhaus, J. Wang, D.-W. Kim, D.D.H. Kim, J. Mayer, Y.-T. Goh, P. le Coutre, N. Takahashi, I. Kim, G. Etienne, D. Andorsky, G.C. Issa, R.A. Larson, F. Bombaci, S. Kapoor, T. McCulloch, K. Malek, L. Yau, S. Ifrah, M. Hoch, J.E. Cortes, and T.P. Hughes, for the ASC4FIRST Investigators*

The NEW ENGLAND JOURNAL of MEDICINE

ASCO and EHA presentations

Official Press Program at ASCO, **given to <1% of abstracts**

Plenary presentation at EHA, as **one of the six best abstracts**

FDA submission under RTOR; global submissions planned H2 2024-2025
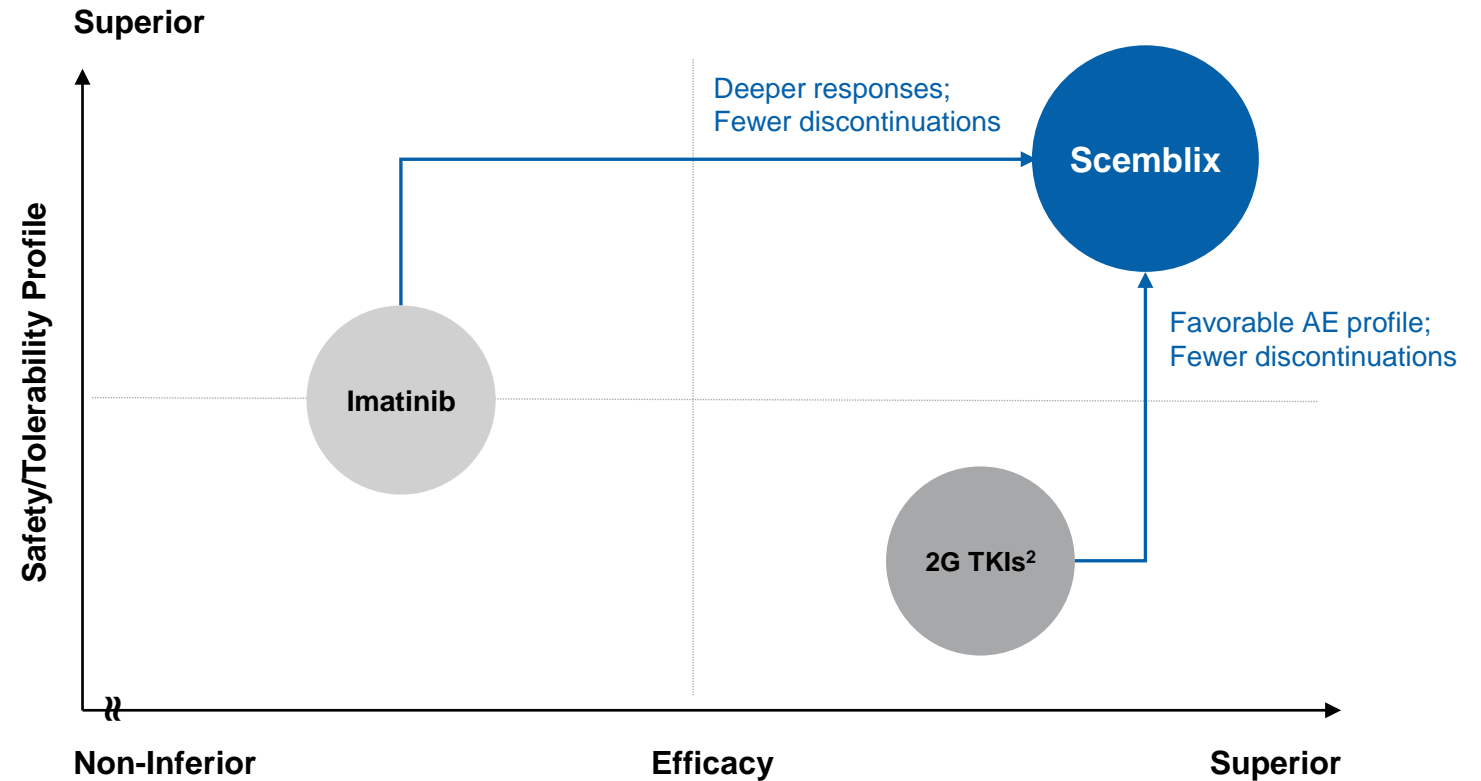

Agenda

1   Novartis legacy in CML and current unmet needs

2   *Scemblix* ASC4FIRST results

3   *Scemblix:* **Establishing the 1L CML treatment of choice**

4   Q&A

ASC4FIRST results position Scemblix to be the treatment of choice for newly diagnosed CML patients upon approval

Superior[1] benefit-risk profile vs SoC TKIs

✓ Better efficacy with fewer AEs and treatment discontinuations

✓ Numerically higher MMR rate vs 2G TKIs

✓ Half the discontinuation rate of imatinib or 2G TKIs

Superior

Deeper responses;
Fewer discontinuations

Scemblix

Safety/Tolerability Profile

Imatinib

Favorable AE profile;
Fewer discontinuations

2G TKIs[2]

Non-Inferior   Efficacy   Superior

1. ASC4FIRST trial met both primary endpoints with clinically meaningful and statistically significant results; Scemblix® (asciminib) shows superior MMR rates at week 48 vs standard-of-care TKIs (imatinib, nilotinib, dasatinib, and bosutinib) in newly diagnosed Ph+CML-CP patients. Investigator selected 2G TKIs – nilotinib, dasatinib, bosutinib.

By combining a differentiated clinical profile with strong execution, Scemblix has been firmly established as the market leader in 3L+
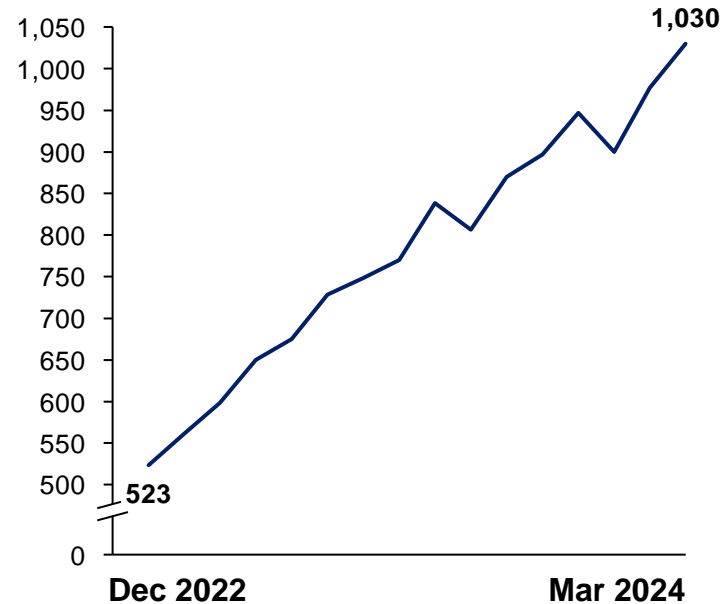
Continued momentum in 3L+

Global sales
USD m, % cc

+83%

	Q1 2023	Q1 2024
Total	76	136
Ex-US	15	48
US	61	88

■ US   ■ Ex-US
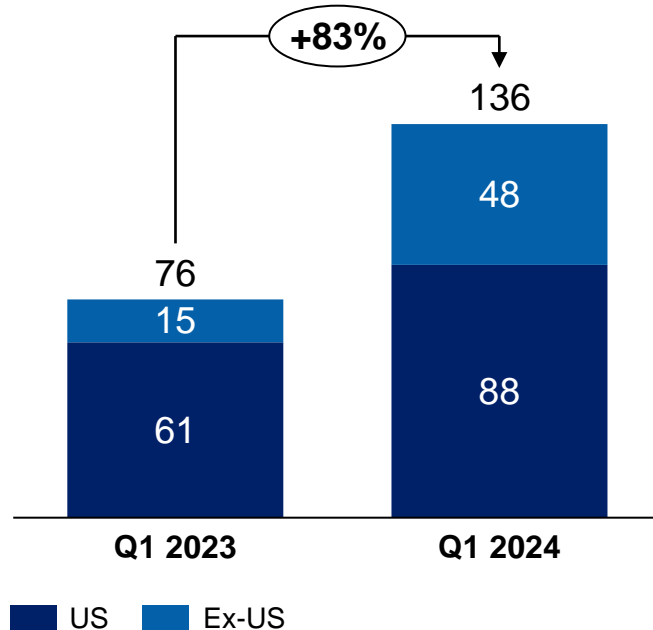
Continued strong growth in monthly prescribers

US total monthly writers
#

1,050
1,000
950
900
850
800
750
700
650
600
550
500
0

523 → 1,030

Dec 2022 — Mar 2024

>2x NBRx share vs any other competitor in 3L+

US 3L+ NBRx share[1]
FY 2023, %

- Scemblix 42%
- Iclusig 6%
- Imatinib 12%
- Tasigna 12%
- Sprycel 14%
- Bosulif 14%
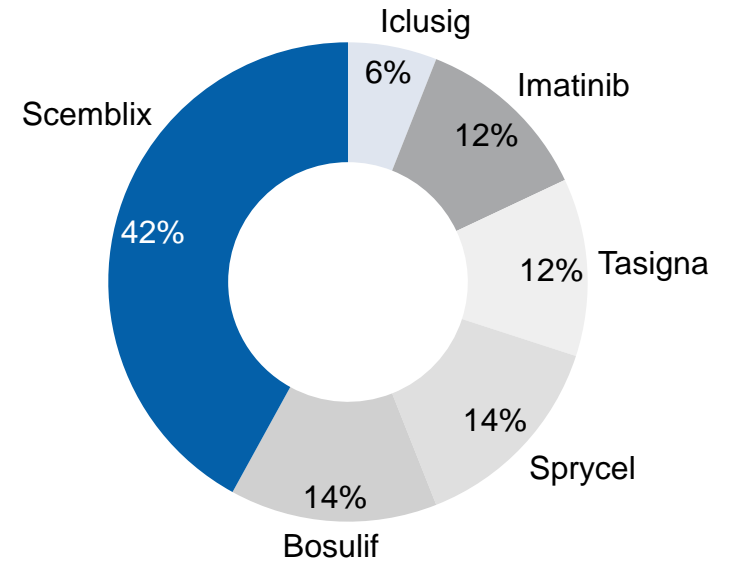
NBRx – new to brand prescription.   1. IQVIA Market Sizing Report, 2024.

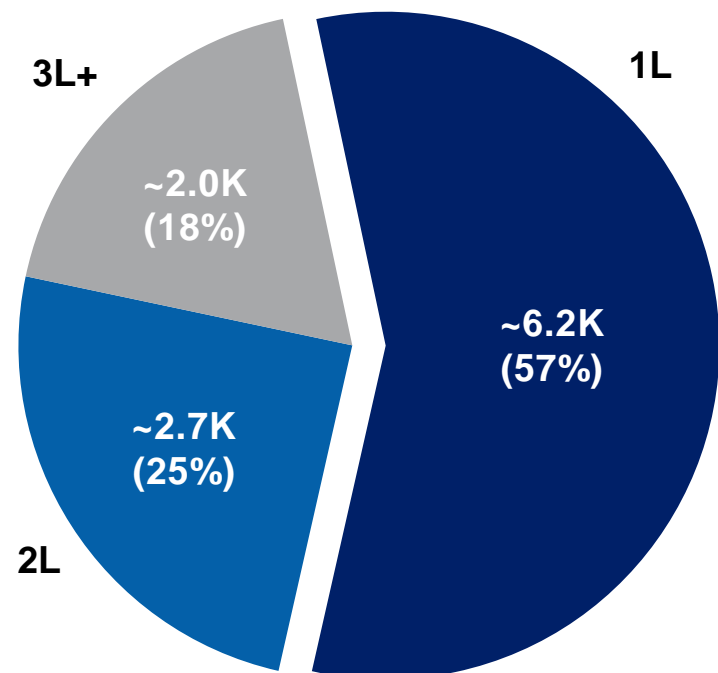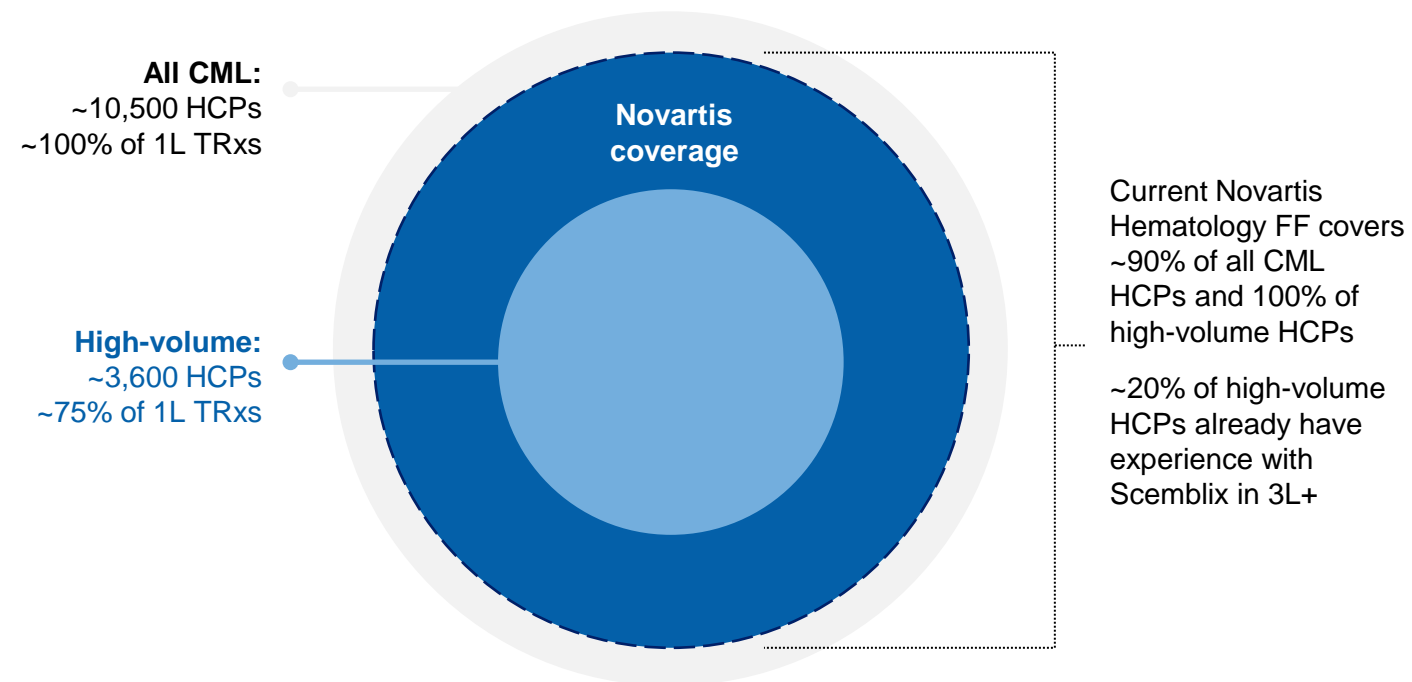# 1L CML opportunity represents ~3x the patient population of 3L+; nearly all prescribers covered by current Novartis Hematology FF

2023 US CML New Patient Population[1]

- **3L+** ~2.0K (18%)
- **2L** ~2.7K (25%)
- **1L** ~6.2K (57%)

US 1L CML Prescriber Population[2]

All CML:
~10,500 HCPs
~100% of 1L TRxs

High-volume:
~3,600 HCPs
~75% of 1L TRxs

Novartis coverage

Current Novartis Hematology FF covers ~90% of all CML HCPs and 100% of high-volume HCPs

~20% of high-volume HCPs already have experience with Scemblix in 3L+

Leveraging our experience in CML to deliver against three critical elements of 1L launch readiness

1

Empower patients
in decision-making

2

Reduce access barriers
to allow optimal care
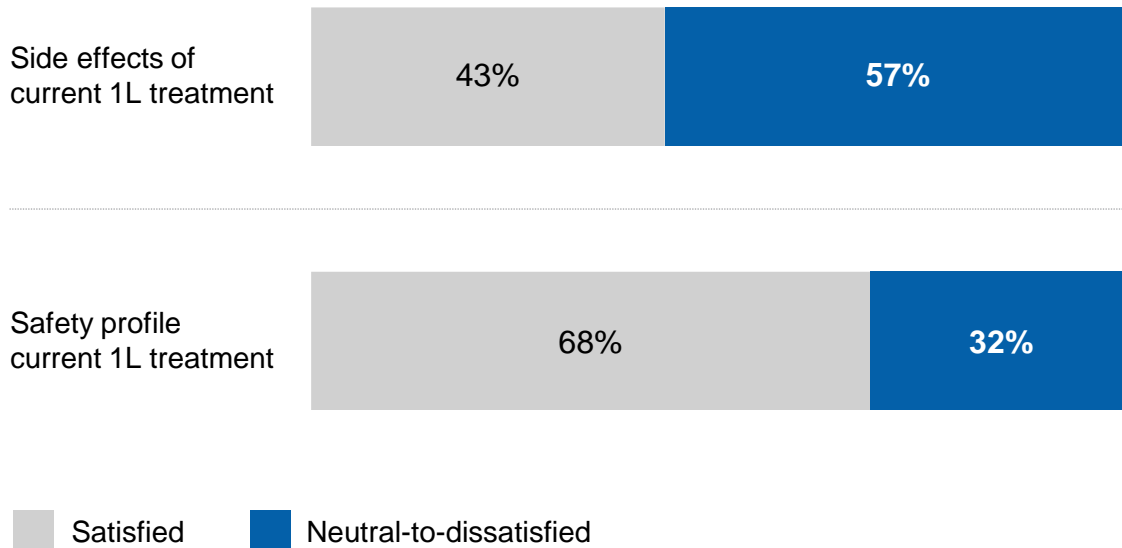
3

Target potential early adopters
on differentiated clinical profile

CML-experienced field sales, market access and medical teams already in place, to appropriately raise awareness of Scemblix clinical profile upon approval

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Empower patients: Elevating the patient perspective on their experience and unmet needs in CML

Many patients are dissatisfied with current treatment options[1]

Side effects of current 1L treatment	43%	57%
Safety profile current 1L treatment	68%	32%

■ Satisfied   ■ Neutral-to-dissatisfied

Empower patients to advocate for a treatment with a tolerability profile that works for them

▶ Develop tools and resources to onboard newly diagnosed patients and support HCP discussion

▶ Continue strong engagement with key patient advocacy groups to facilitate active patient/HCP shared treatment decision-making

▶ Amplify conversations in the community among treatment-naive patients via CML advocates

1. Novartis ATU market research (April 2024).

(2) Reduce access barriers: CML is a managed category, presenting challenges and opportunities for Scemblix anticipated launch

Challenges

- ~40% of covered lives are managed by payers today (PAs, preferred brands, and/or step edits)
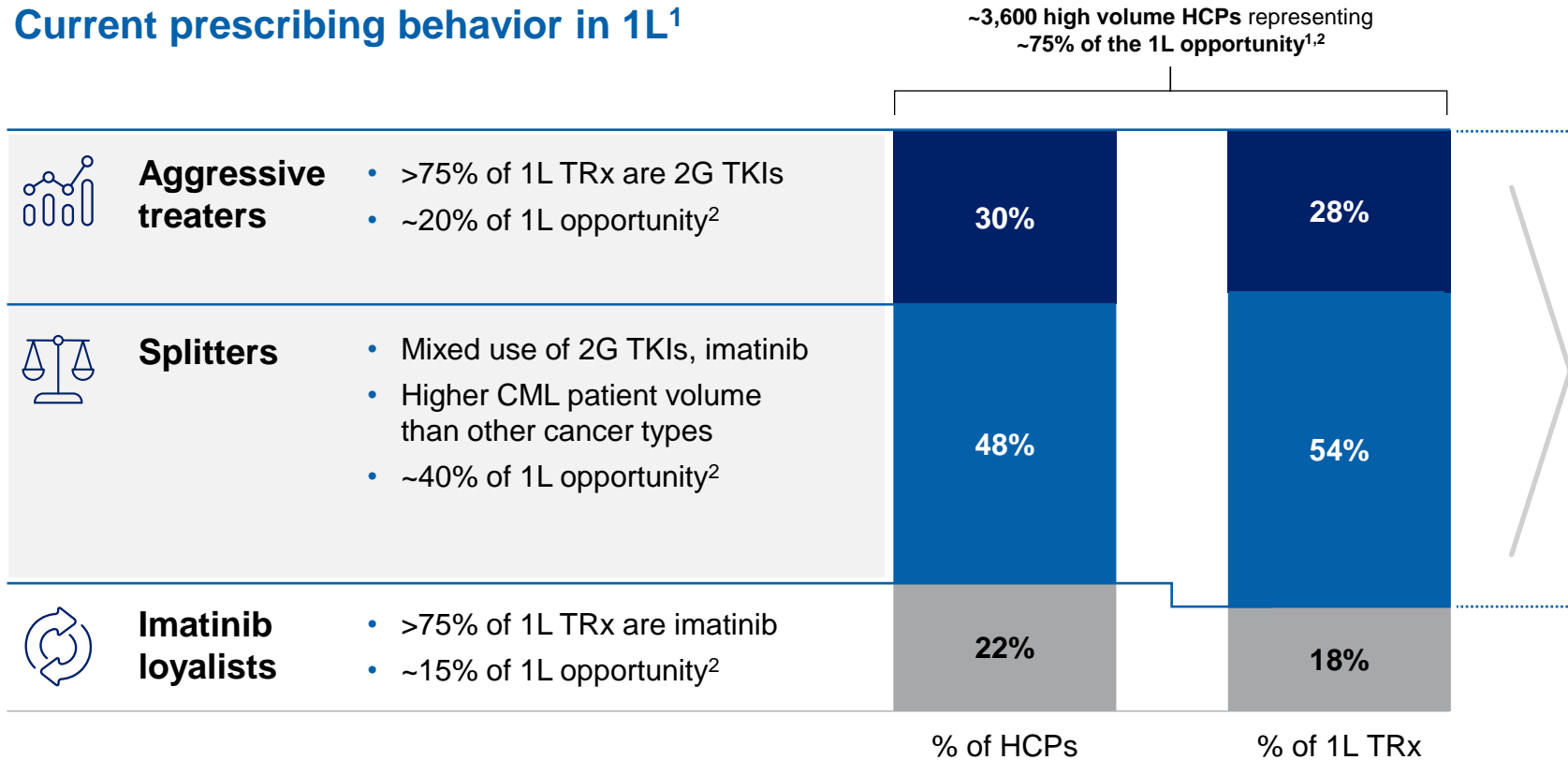- 2G TKIs expected to lose exclusivity in 2024-2025

Opportunities

- HCPs accustomed to advocating for coverage and gaining payer approvals
- Less branded competition

Imperatives for a successful launch

- **Highlight value proposition** with population health decision-makers and payers to support 1L coverage upon approval
- **Educate HCPs about coverage**, PA criteria, and supporting data to foster successful approvals
- **Ensure robust patient services** to minimize patient OOP cost burden, facilitate on-boarding, and provide ongoing support

Target potential early adopters: Understanding ingrained behaviors, initial focus on physicians representing ~60% of 1L opportunity at launch

Current prescribing behavior in 1L[1]

~3,600 high volume HCPs representing
~75% of the 1L opportunity[1,2]

		% of HCPs	% of 1L TRx
Aggressive treaters	• >75% of 1L TRx are 2G TKIs • ~20% of 1L opportunity[2]	30%	28%
Splitters	• Mixed use of 2G TKIs, imatinib • Higher CML patient volume than other cancer types • ~40% of 1L opportunity[2]	48%	54%
Imatinib loyalists	• >75% of 1L TRx are imatinib • ~15% of 1L opportunity[2]	22%	18%

Key attributes of Scemblix prescribers at launch

- Understand tolerability as an unmet need
- Prioritize efficacy but dose adjust for AEs
- Willing to advocate for coverage

1. Novartis internal market research and claims analysis (2023, 2024). 2. Aggressive treaters (~20%), Splitters (~40%), and imatinib loyalists (~15%) make up the ~75% of the 1L TRxs prescribed by ~3600 high-volume HCPs. The remaining ~25% 1L TRxs are widely distributed across ~7000 other HCPs who also treat CML patients (please refer to slide 27).

Differentiated clinical profile, strong commercial readiness and a long patent life sets up Scemblix as a key growth driver for the future

Differentiated clinical profile

- ✓ Better efficacy with fewer AEs and treatment discontinuations
- ✓ Numerically higher MMR rate vs 2G TKIs[1]
- ✓ Half the discontinuation rate of imatinib or 2G TKIs[1]

Strong commercial readiness

- ✓ Deep disease expertise
- ✓ Strong engagement with CML experts and patients
- ✓ Field teams already in place
- ✓ Targeted approach at launch

Long patent protection in a rare disease population

- ✓ US compound patent plus expected PTE until 2035[2]
- ✓ FDA Orphan Drug Designation granted for treatment of CML[3]
- ✓ Excluded from IRA negotiations as a rare disease therapy

Confident in Scemblix USD 3bn+ global peak sales across lines

IRA – Inflation Reduction Act.   1. Investigator selected 2G TKIs – nilotinib, dasatinib, bosutinib.   2. US compound patent expires in 2033, with expected PTE to 2035. In Europe, compound patent also expires 2033 with additional SPC to 2037 (still pending in some jurisdictions).   3. Granted in 2017.

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Better benefit-risk profile vs current SoC TKIs positions Scemblix as a potential therapy of choice for newly diagnosed CML patients upon approval

Scemblix demonstrated superior efficacy...

✓ Superior MMR rates vs IS-TKIs and vs imatinib alone

✓ Consistent results regardless of baseline characteristics

✓ Earlier achievement of MMR and greater depth of responses

✓ Improvement vs 2G TKI[1] in MMR rate, speed and depth of responses

...with a favorable safety and tolerability profile

✓ Fewer grade ≥3 AEs

✓ Fewer dose adjustments/interruptions needed to manage AEs

✓ Half the rate of all-grade AEs leading to discontinuation

✓ Lower rates and severity of most AEs associated with 2G TKI[1] class and impacting patient lives

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"Scemblix is the first CML treatment to show significantly better efficacy compared to investigator-selected standard-of-care TKIs. When you combine superior response with the excellent safety and tolerability profile of Scemblix, we have a very promising potential frontline option for newly diagnosed patients to support them in achieving their treatment goals."
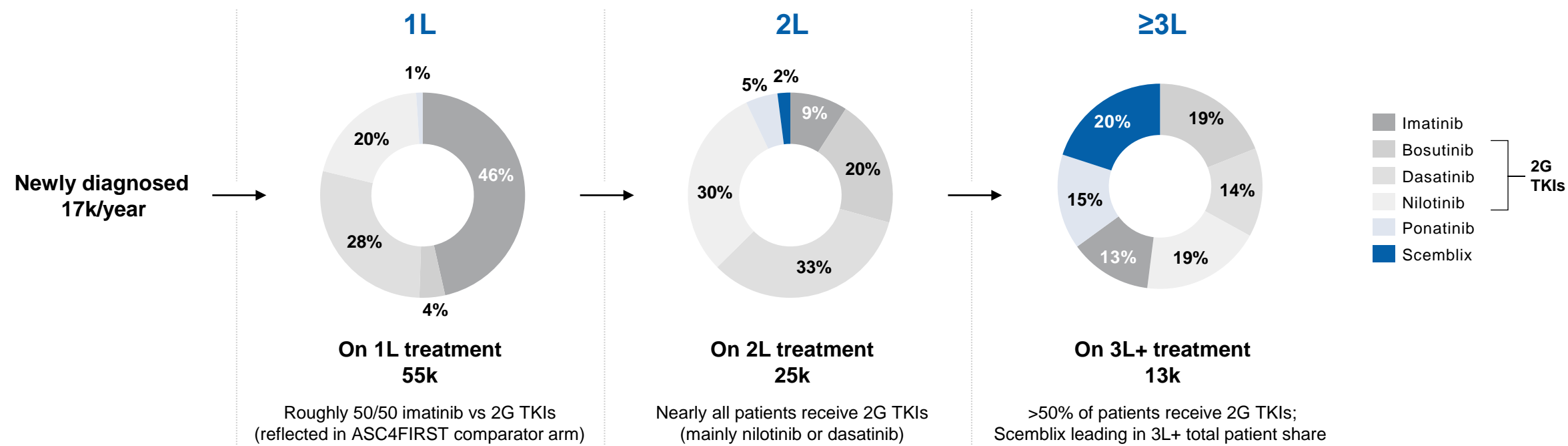
Prof. Tim Hughes, MD,
South Australian Health & Medical Research Institute (SAHMRI)
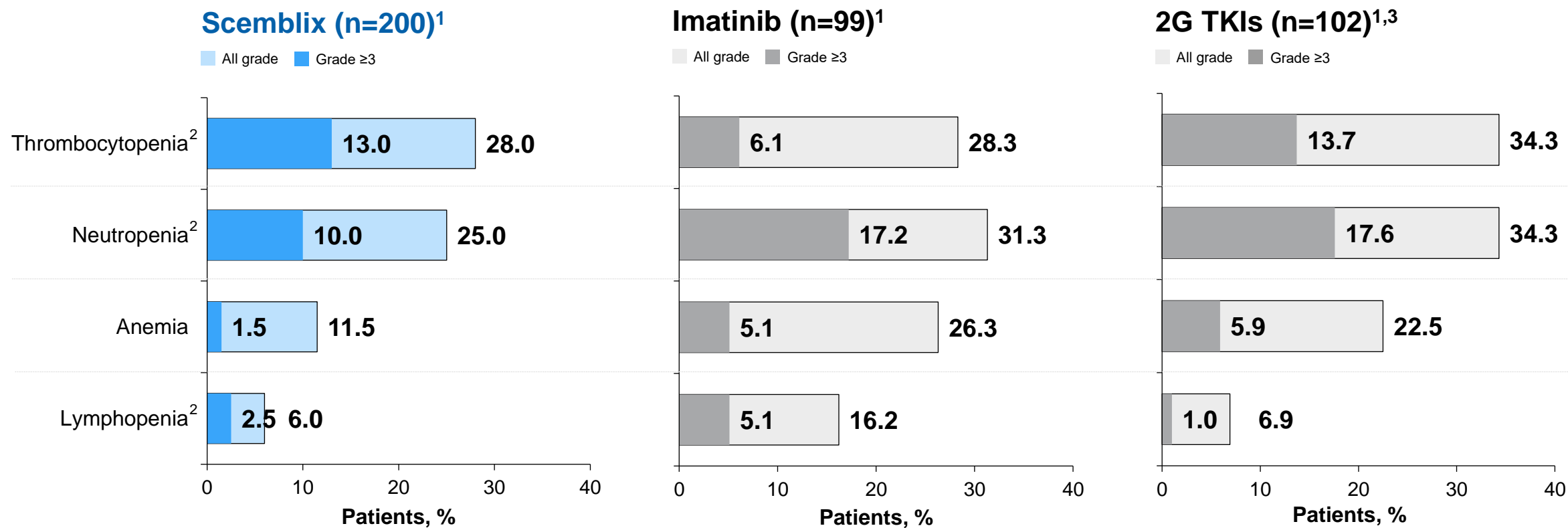
Appendix

Current treatment landscape for 1L CML is roughly evenly split between imatinib and 2nd generation (2G) TKIs

CML treatment landscape in G7[1,2,3]

1L

2L

≥3L

Newly diagnosed 17k/year

1L chart:
- 46%
- 1%
- 20%
- 28%
- 4%

2L chart:
- 9%
- 5%
- 2%
- 20%
- 33%
- 30%

≥3L chart:
- 20%
- 19%
- 14%
- 19%
- 13%
- 15%

On 1L treatment 55k

On 2L treatment 25k

On 3L+ treatment 13k

Roughly 50/50 imatinib vs 2G TKIs (reflected in ASC4FIRST comparator arm)

Nearly all patients receive 2G TKIs (mainly nilotinib or dasatinib)

>50% of patients receive 2G TKIs; Scemblix leading in 3L+ total patient share

Legend:
- Imatinib
- Bosutinib
- Dasatinib
- Nilotinib
- Ponatinib
- Scemblix

2G TKIs (Bosutinib, Dasatinib, Nilotinib)

Most hematologic toxicities occurred at lower severities with Scemblix vs imatinib and 2G TKIs

Scemblix (n=200)[1]
- All grade
- Grade ≥3

Imatinib (n=99)[1]
- All grade
- Grade ≥3

2G TKIs (n=102)[1,3]
- All grade
- Grade ≥3

	Scemblix Grade ≥3	Scemblix All grade	Imatinib Grade ≥3	Imatinib All grade	2G TKIs Grade ≥3	2G TKIs All grade
Thrombocytopenia[2]	13.0	28.0	6.1	28.3	13.7	34.3
Neutropenia[2]	10.0	25.0	17.2	31.3	17.6	34.3
Anemia	1.5	11.5	5.1	26.3	5.9	22.5
Lymphopenia[2]	2.5	6.0	5.1	16.2	1.0	6.9

Patients, %

References

Page 4 – Current unmet need:

1. Cortes JE et al. J Hematol Oncol. 2021;14(1):44.   2. Hochhaus A, et al. Leukemia. 2016;30:1044-54.   3. Cortes JE, et al. J Clin Oncol. 2016;34:2333-40.   4. Brummendorf TH, et al. Blood. 2020;136(suppl 1):41–42.   5. Kota V, et al. Presented at: ASH 2023; San Diego, CA, and virtual. Poster 5190.   6. Hughes TP, et al. Leukemia. 2017; 31: 2529–2531. Refers to patients who were without MR4.5 at the time of switch and subsequently did not achieve MR4.5 on their second therapy   7. Cortes JE, et al. Am J. Hematol. 2019; 94:346–357.   8. Haznedaroglu IC. Mediterr J Hematol Infect Dis. 2015;7(1):e2015014.   9. Rychter A, et al. Med Oncol. 2017;34:104

Page 6 – BCR ABL binding and Scemblix design:

References for Scemblix design: Manley PW, et al. Leukemia Research. 2020; 98:106458.   ASCEMBL Ph3 week 96: Hochhaus A. et al., Leukemia 2023; 37:617–626. Wylie AE, et al. Nature 2017; 543:733-737.   Schoepfer J, et al. J Med Chem. 2018;61:8120-8135.

References for BCR-ABL figure: Wylie AA, et al. Nature. 2017;543:733-737.   Schoepfer J, et al. J Med Chem. 2018;61:8120-8135.   Hughes TP, et al. Oral presentation at: 25th EHA Virtual Annual Meeting; June 11-21, 2020. Abstract S170.   Manley PW, et al. Leuk Res. 2020;98:106458.   Nagar B, et al. Cell. 2003;112:859-871.   Hantschel O, et al. Cell. 2003;112:845-857.   Colicelli J. Sci Signal. 2010;3:re6.   Hantschel O. Genes Cancer. 2012;3:436-446.

References for dendrograms: Steegmann JL, et al. Leuk Lymphoma. 2012;53:2351-61.   Karaman MW, et al. Nat Biotechnol. 2008;26:127-32.   Lang JD, et al. Clin Cancer Res. 2018;24:1932-43.   Remsing Rix LL, et al. Leukemia. 2009;23:447-85.   Bosutinib inhibits additional kinases that are not depicted in the dendrogram.

Page 14 – 1L unmet need:

4. Kota V, et al. Presented at: ASH 2023; San Diego, CA, and virtual. Poster 5190.   5. Cortes JE, et al. *J Clin Oncol.* 2016;34(20):2333-2340.   6. Hochhaus A, et al. *Leukemia.* 2016;30(5):1044-1054.   7. Brümmendorf TH, et al. *Leukemia.* 2022;36:1825-1833.   8. Rychter A, et al. Med Oncol. 2017;34:104