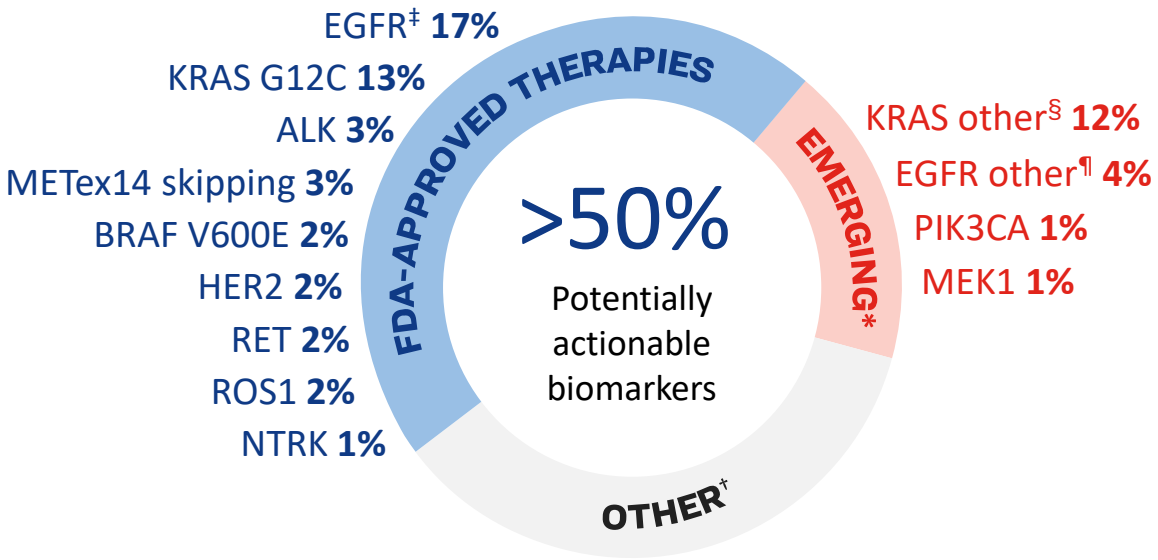
OPTIMIZING TESTING AND SELECTION OF FIRST-LINE THERAPY IN NSCLC

Genomic Testing Identifies Actionable Biomarkers in NSCLC

Biomarkers in Lung Adenocarcinoma[1-11]



*Biomarkers with therapies under investigation but not yet approved. †Unknown oncogenic driver detected. ‡*EGFR*-sensitizing mutations including exon 20 insertions. §All *KRAS* mutations other than *KRAS* G12C. ¶Secondary *EGFR* mutations, including Thr790Met and Cys797Ser, and other less common *EGFR* mutations.

ALK = anaplastic lymphoma kinase; BRAF = v-raf murine sarcoma viral oncogene homolog B; EGFR = epidermal growth factor receptor; HER2 = human epidermal growth factor receptor 2; KRAS = Kirsten rat sarcoma; MEK1 = dual specificity mitogen-activated protein kinase kinase 1; MET = mesenchymal-epithelial transition factor; NSCLC = non–small cell lung cancer; NTRK = neurotrophic tyrosine receptor kinase; PIK3CA = phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha; RET = rearranged during transfection; ROS1 = ROS proto-oncogene 1.

References available in speaker notes.

Approximately Half of All Patients With NSCLC Undergo Comprehensive Testing

Biomarker Testing Results Available Prior to 1L Treatment in US Community Oncology Centers, 2020-2022	
Testing rates in advanced NSCLC (n=582), n (%)	
Patients with any biomarker testing results by any method available prior to 1L treatment, n	461
*ALK**	355 (77.0)
*BRAF**	335 (72.7)
*EGFR**	371 (80.5)
*KRAS**[†]	294 (63.8)
*MET**	328 (71.1)
*NTRK**	253 (54.9)
PD-L1*	388 (84.2)
*RET**	305 (66.2)
*ROS1**	344 (74.6)
NGS testing was ordered prior to 1L treatment for 54.6% of patients.	

Data from MYLUNG.

*Denominator: patients with biomarker testing results prior to 1L treatment. [†]*KRAS* testing is approved for later-line treatment.
NGS = next-generation sequencing; PD-L1 = programmed death-ligand 1; 1L = first line.
Evangelist M, et al. Poster presented at: ASCO 2023. Abstract 9109.

Treatment Patterns in Advanced NSCLC

Use of Targeted Therapy in Patients With NSCLC

Flatiron Analysis of 1L Targeted Therapy Usage in Patients With Positive Biomarker Status on or Prior to Therapy Initiation, 2020-2022

	Patients With Positive Biomarker Status, n	Patients Who Received Targeted Therapy, n	Patients Who Received Targeted Therapy, %
ALK	220	175	79.5
EGFR	1439	1134	78.8
ROS1	71	52	73.2
RET	57	29	50.9
MET	174	78	44.8
NTRK	14	6	42.9
BRAF	424	57	13.4

For rarer biomarkers like *RET*, identifying an actionable alteration may only lead to use of the appropriate targeted therapy about half the time.

Data on file. Eli Lilly and Company; 2023.

Administration of 2L Therapy in Patients With Advanced NSCLC Who Received 1L Therapy

Flatiron Analysis of 1L and 2L Therapy Usage in Patients With Positive Biomarker Status Prior to Therapy Initiation, 2020-2022[1,2]

n (%)	*RET* Fusion–Positive Cohort (n=46)	*RET* Fusion–Negative Cohort (n=5761)
Any 1L therapy	46 (100)	5761 (100)
Any 2L therapy	23 (50)	3173 (55)

CORRELATE Analysis of 2L and 3L Therapy Use in Flatiron Health Data From Patients With Metastatic NSCLC Receiving 1L IO ± CT, 2016-2021[3]

Therapy	Patients, n (%)
1L therapy	682 (100)
2L therapy	275 (40.3)
Death prior to 2L therapy	256 (37.5)
PD with no 2L therapy	50 (7.3)
Excluding patients who were alive without documented PD after 1L treatment, of the remaining 581 patients, only 275 (47.3%) received any 2L treatment.	
3L therapy	106 (15.5)

~40%-50% of patients with advanced NSCLC who receive 1L therapy do not receive 2L therapy.[1-5]

CT = chemotherapy; IO = immuno-oncology; PD = progressive disease; 2L = second line; 3L = third line.

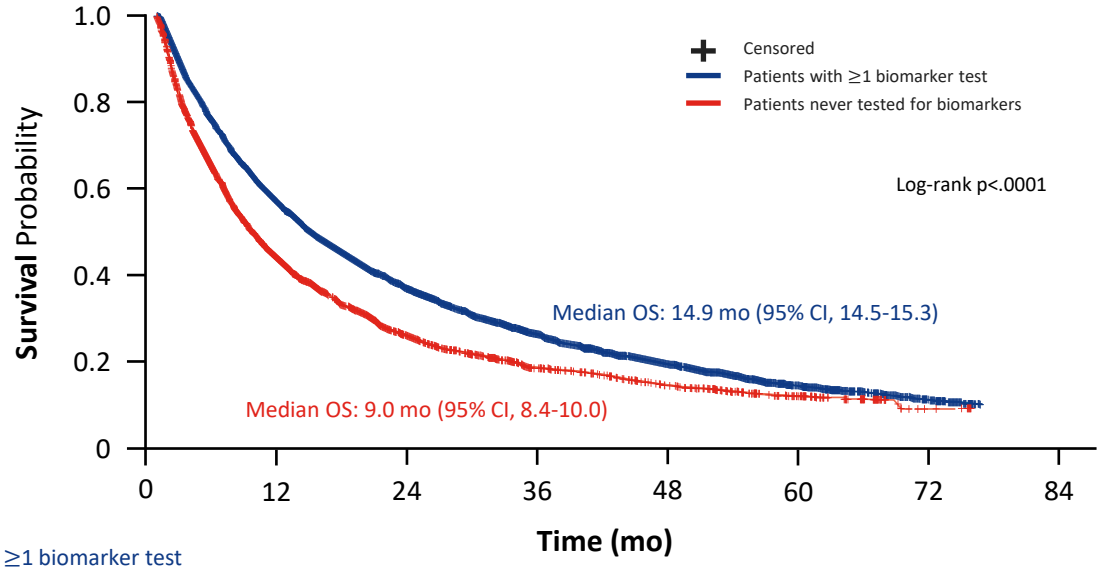
1. Data on file. Eli Lilly and Company; 2023. 2. Hess LM, et al. *BMC Cancer*. 2021;21:28. 3. Liu SV, et al. Poster presented at: ELCC 2024. Poster 90P. 4. Davies J, et al. *PLoS One*. 2017:0175679. 5. Bazhenova L, et al. *Cancer Treat Res Commun*. 2022:33;100637.

Biomarker Testing Prior to Initiating 1L Therapy Is Important

Improved Survival Outcomes Are Observed With Biomarker Testing and Receipt of Guideline-Concordant Therapy

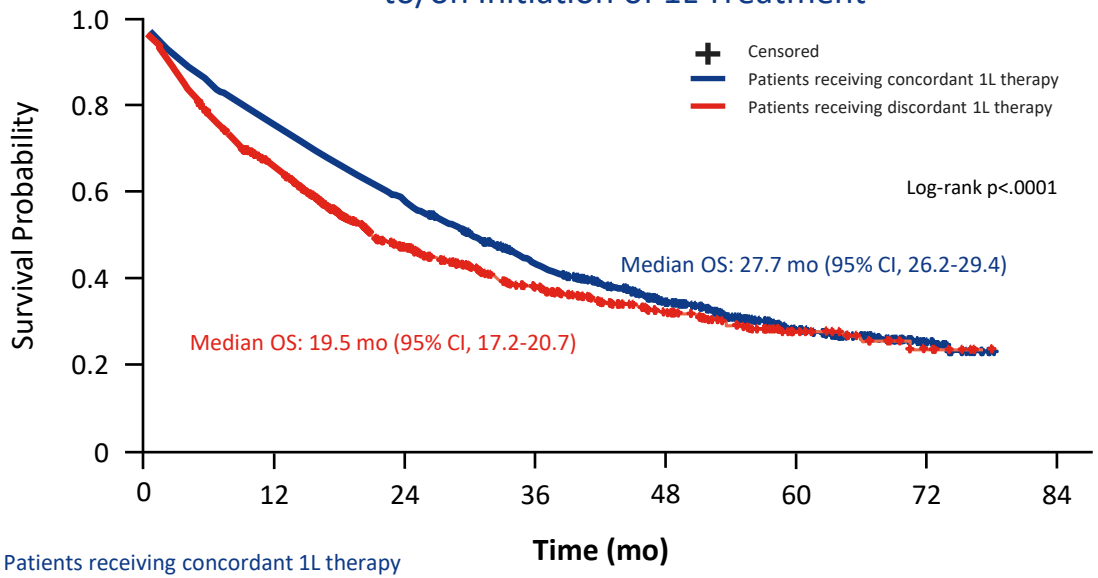
Kaplan-Meier Curves of OS Among Patients by Testing Status

OS in Patients With ≥1 Test vs Never Tested



≥1 biomarker test	19,041	8483	4353	2264	1087	443	107	0
Never tested for biomarkers	2531	823	374	180	103	45	7	0

OS for Patients Receiving Concordant vs Discordant 1L Treatment After Testing Positive for a Biomarker Prior to/on Initiation of 1L Treatment

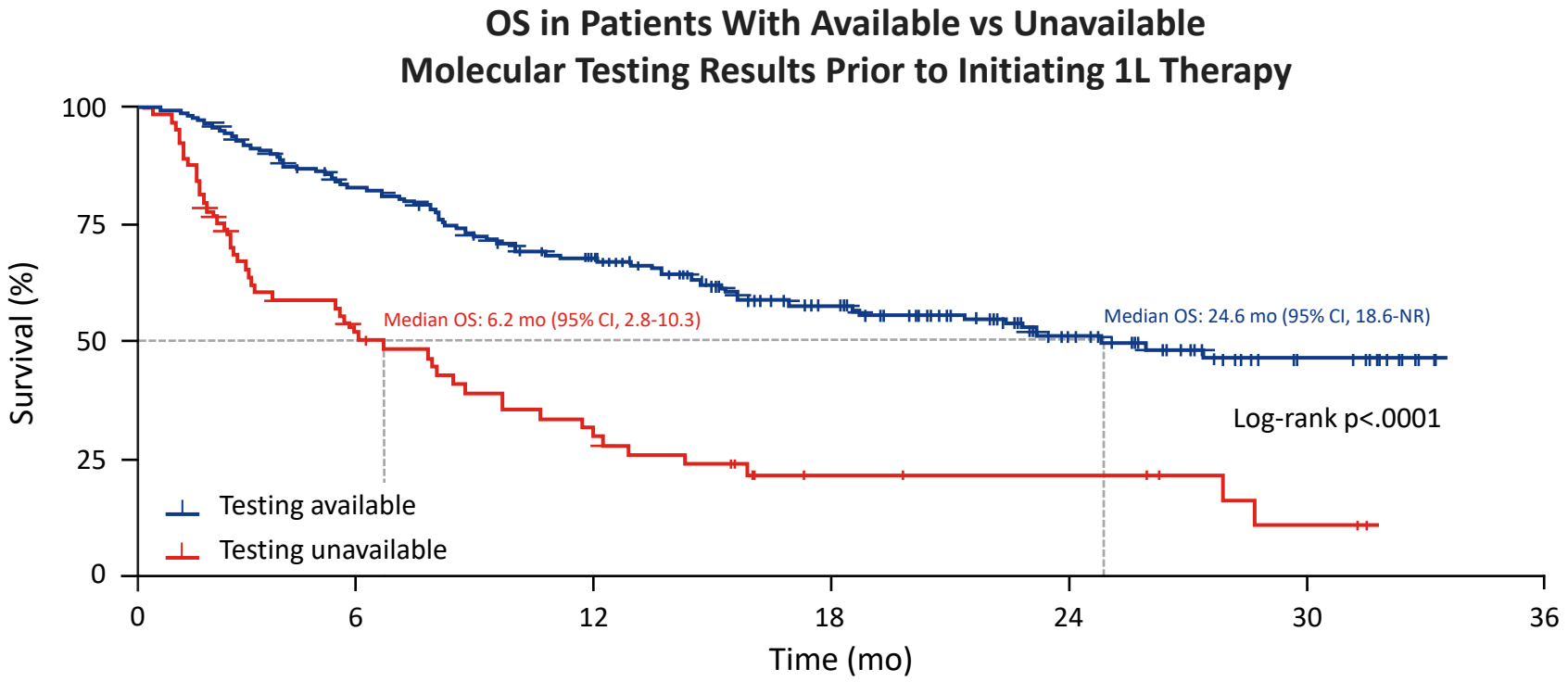


Patients receiving concordant 1L therapy	2609	1593	870	439	204	81	22	0
Patients receiving discordant 1L therapy	900	433	227	130	69	27	7	0

OS = overall survival.

Bhandari NR, et al. *J Natl Comp Canc Netw*. 2023;21(9):934-944.

Availability of Molecular Genotyping Results Before 1L Therapy Initiation Was Associated With Better OS



Testing available	261	206	154	91	42	14	0
Testing unavailable	65	27	14	7	6	2	0

Aggarwal C, et al. *JCO Precis Oncol*. 2023;7:e2300191.

Switching to Targeted Therapy When an Actionable Biomarker Is Detected After Initiating 1L Therapy

Test, Wait, Treat for Optimal Patient Outcomes

Every patient deserves:

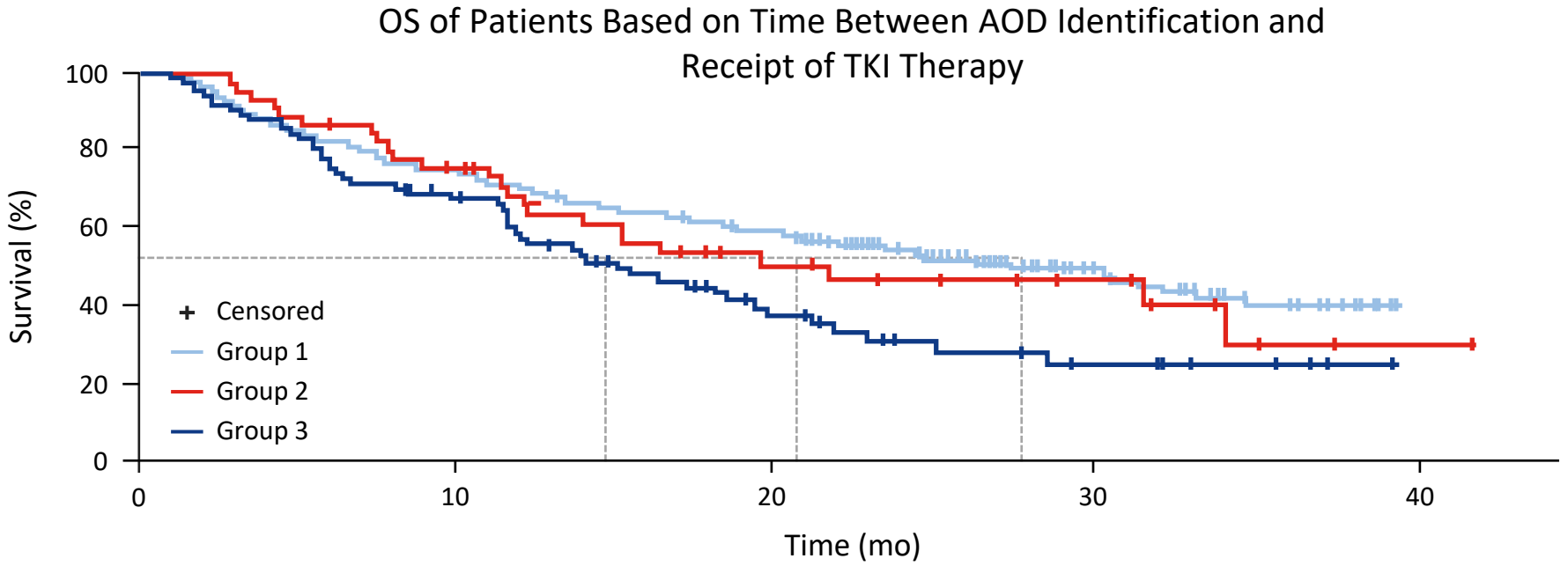
To be tested

To wait for the results

To use the results to determine therapy

If you can’t wait, consider starting with chemotherapy, then switching to targeted therapy once test results are known.

Patients With Actionable Oncogenic Drivers Who Received Therapy After Receipt of Genomic Testing Results Showed an OS Benefit vs Those Treated Before Results



	Group 1 (N=379)	Group 2 (N=47)	Group 3 (N=84)	Group 2+3 (N=131)
OS				
Median (95% CI, mo)	28.8 (23.3-34.6)	21.7 (12.2-NR)	15.3 (11.5-19.7)	16.5 (12.2-21.7)
HR	Reference	1.12	1.62	1.27
P value	–	.59	.003	.27

Group 1

Patients treated after report of AOD

Group 2

Patients treated before report of AOD, then switched to TKI within 35 days

Group 3

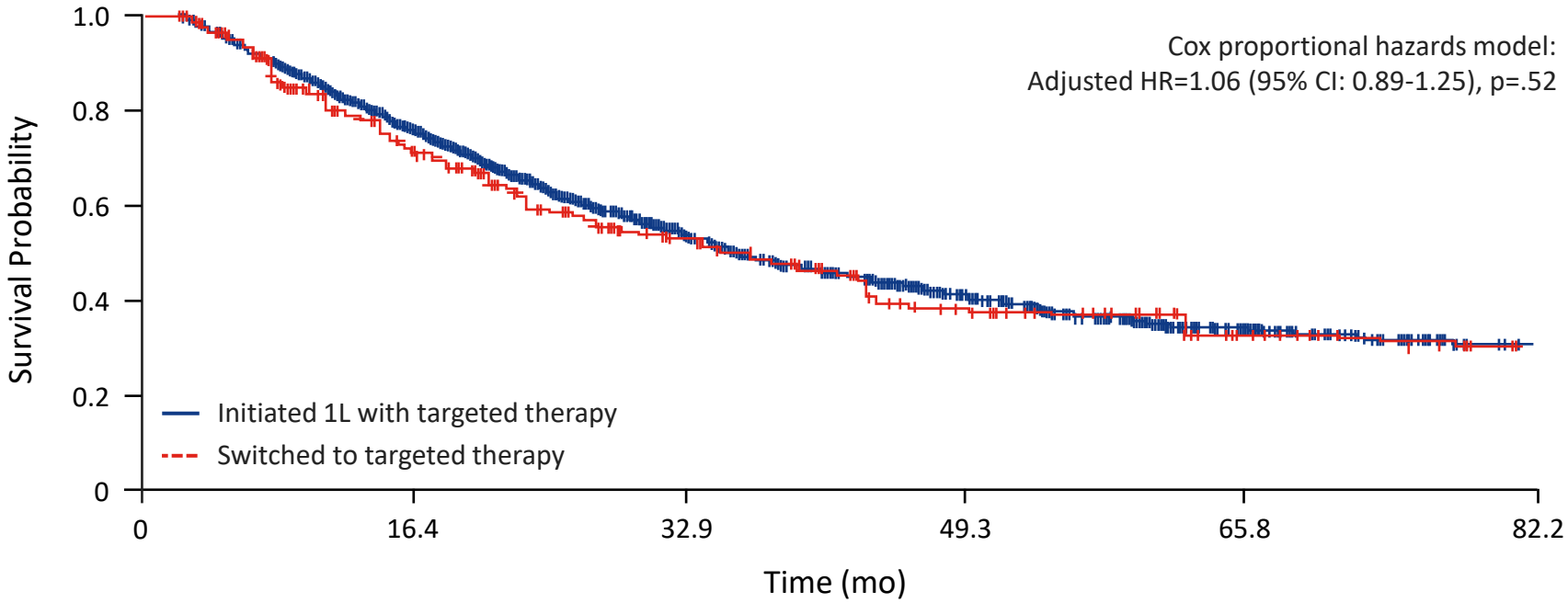
Patients treated before report of AOD who were not switched to TKI within 35 days

AOD = actionable oncogenic driver; HR = hazard ratio; NR = not reached; TKI = tyrosine kinase inhibitor.

Scott JA, et al. *JCO Oncol Pract*. 2023;20(1):145-153.

Survival Outcomes Are Similar for Patients Who Initiate Targeted Therapy vs Chemotherapy With Early Switch to Targeted Therapy

OS Among Patients by Initial vs Early Switch to 1L Targeted Therapy*



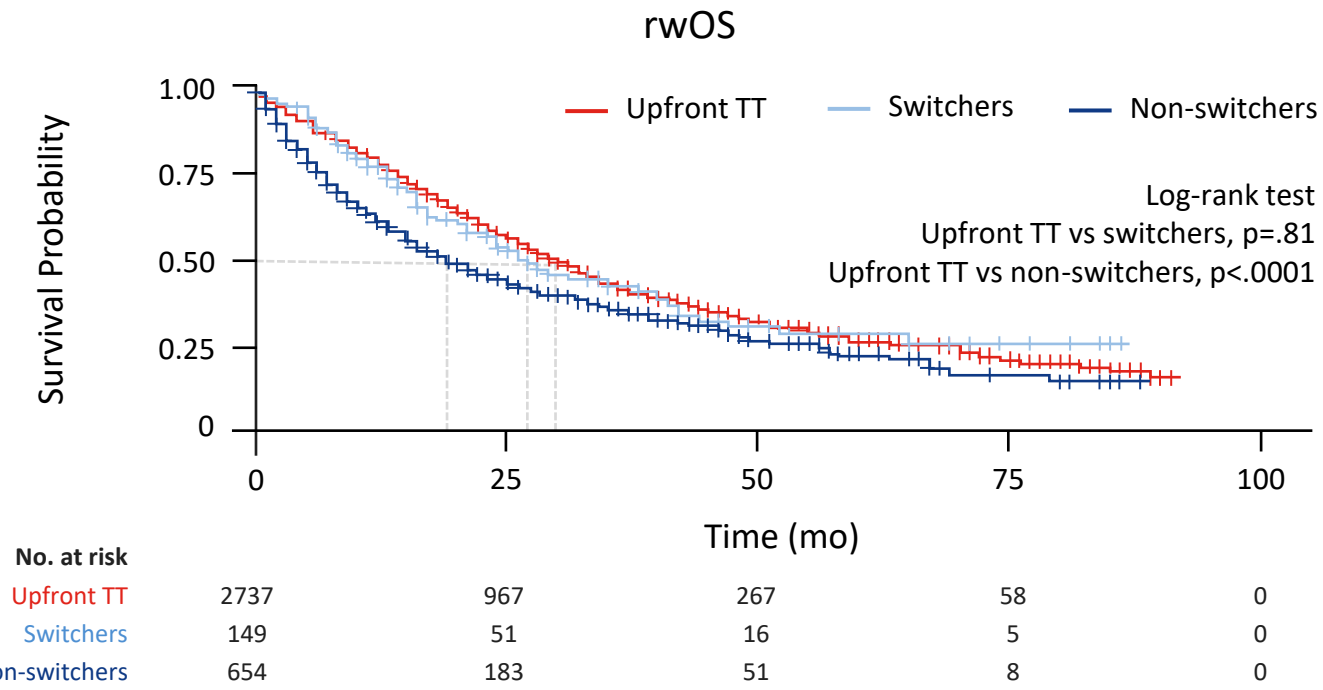
Initiated 1L with targeted therapy	3107	1923	994	445	164	0
Switched to targeted therapy	346	178	101	37	13	0

*Early switch to targeted therapy was defined as those who switched from CT to targeted therapy within the first 56 days of receiving 1L therapy.

Hess LM, et al. *Cancer Treat Res Comm*. 2023;37:100761

More Information

Improved Survival Outcomes Are Observed With Early Switch to Targeted Therapy



No. at risk					
Upfront TT	2737	967	267	58	0
Switchers	149	51	16	5	0
Non-switchers	654	183	51	8	0

	Duration of Follow-up, Median (IQR) mo	rwOS, Median (95% CI), mo	Adjusted HRs
Upfront TT N=2737	17 (8-32)	30 (28-32)	Reference group
Switchers N=149	16 (8-33)	27 (21-40)	0.9697 p=.8002
Non-switchers N=654	11 (4-26.75)	19 (16-23)	1.3673 p=.0000

IQR = interquartile range; rwOS = real-world overall survival; TT = targeted therapy.
Stricker T, et al. *Oncologist.* 2024:1-9.

Summary

Biomarker testing and receipt of guideline-concordant therapy can lead to improved survival outcomes in patients with NSCLC[1]

- Only 40%-50% of patients with NSCLC receive 2L therapy[2-6]

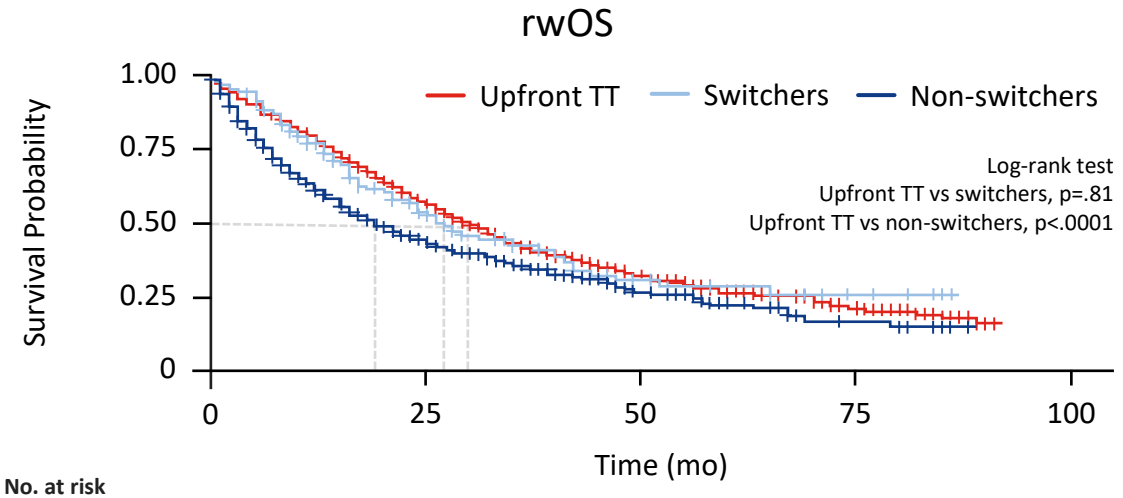
Receipt of molecular testing results prior to initiation of 1L therapy is advantageous[1,7]

Patients who initiate CT prior to receipt of molecular testing results may benefit from switching to targeted therapy when results are available[8-10]

- Switching to targeted therapy by Days 35, 56, and 42-84 showed no disadvantage compared to upfront targeted therapy [8-10]

References available in speaker notes.

Improved Survival Outcomes Are Observed With Early Switch to Targeted Therapy



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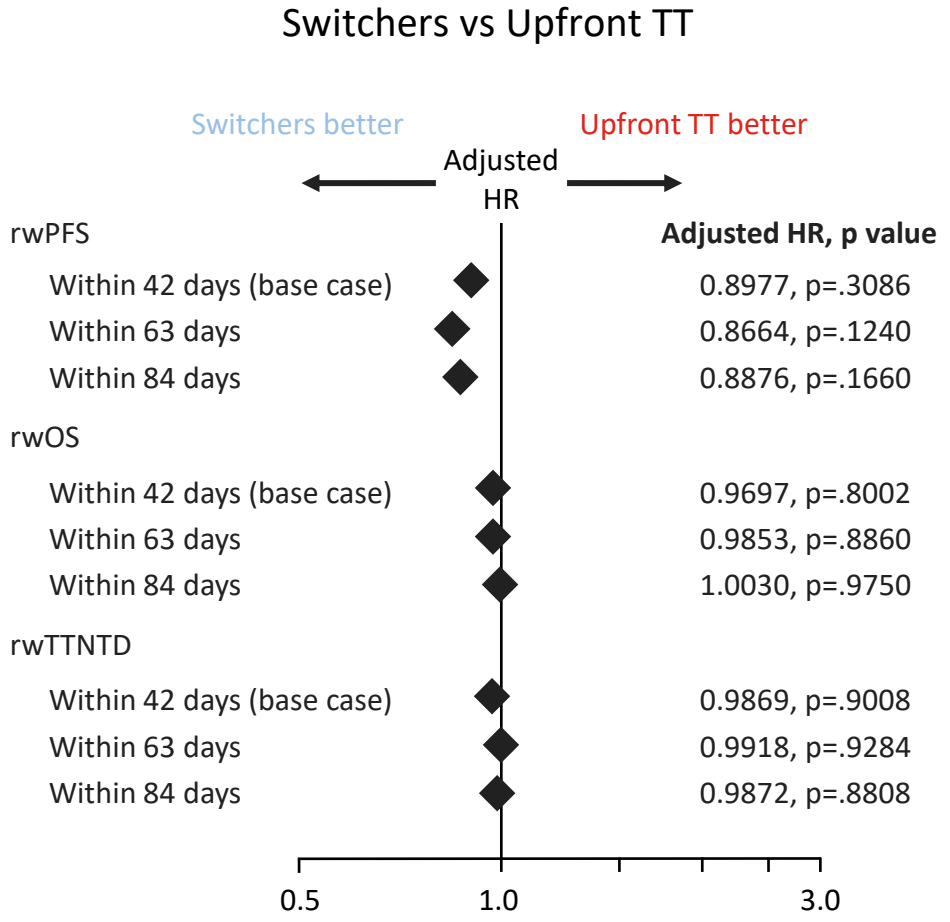

IQR = interquartile range; rwOS = real-world overall survival; rwPFS = real-world progression-free survival; rwTTNTD = real-world time to next treatment or death; TT = targeted therapy.

Stricker T, et al. *Oncologist*. 2024:1-9.