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INTRODUCTION

The introduction of immunotherapy and tyrosine kinase inhibitors (TKI) in metastatic non-small cell lung cancer (NSCLC) has significantly improved survival and changed the standard of care in this group of patients. However, acquired resistance develops in most patients. The addition of local therapy such as radiotherapy (RT) may improve disease control and extend time on systemic therapy in selected patients. We aimed to evaluate outcomes following targeted RT in oligoprogressive NSCLC in a tertiary cancer centre.

METHODS

Patients who received RT for oligoprogressive NSCLC between 2016 – 2025 were retrospectively identified from our institutional database. Oligoprogression was defined as 5 or fewer progressive lesions. Patients who did not receive systemic therapy at the time of RT were excluded. Patient demographics, clinical and treatment parameters were extracted. Systemic therapy was categorised as TKI and chemotherapy +/- immunotherapy (C-IO). Primary end-point was time-to-next systemic therapy (TTNS) defined from the start of RT until the start of next systemic therapy. Secondary end-points included progression-free survival (PFS) and overall survival (OS) which were defined from the start of RT until disease progression or death, and death from any cause, respectively. TTNS, PFS and OS were estimated using Kaplan-Meier method and compared using log rank test. The reverse Kaplan-Meier method was used to estimate the median follow-up time.

RESULTS

A total of 35 patients were included: 22 (63%) patients were on TKI and 13 (37%) on C-IO. See **Table 1** for baseline characteristics. All patients had RT to 1-2 sites with the majority being bone, brain and lung metastases. About half of the patients were treated with SBRT or SRS technique (**Table 1**). The median duration that patients were on TKI and C-IO before RT were 1.1 years (IQR 0.9 – 2.0) and 0.6 years (IQR 0.4 – 0.7, $p=0.013$), respectively. Median follow-up for the whole cohort was 5.7 years (95% CI 3.2 – NE). In the TKI cohort, 11/22 (50%) patients changed systemic therapy after RT, with a median TTNS of 1.5 years (95% CI 0.7 – NE). In the C-IO cohort, 9/13 (69%) patients changed systemic therapy after RT, with a median TTNS of 1.0 year (95% CI 0.4 – NE) (**Figure 2**). Median PFS were 0.8 years (95% CI 0.4 – 1.2) and 0.5 years (95% CI 0.2 – 2.0) in the TKI and C-IO cohorts ($p=0.838$), respectively. Median OS were 2.1 years (95% CI 1.3 – 2.4) and 3.5 years (1.1 – 5.7), in the TKI and C-IO cohorts ($p=0.186$), respectively. Nine (41%) patients in the TKI cohort and 9 (69%) in the C-IO cohort received additional RT for subsequent disease progression.

Table 1: Patient & RT treatment characteristics

Patient characteristics	All patients N=35	TKI N=22	Chemo ± IO N=13	p-values
Median age (IQR)	62 (53-69)	60 (53-69)	64 (58-68)	0.733
Gender				0.022
Male	21 (60%)	10 (46%)	11 (85%)	
Female	14 (40%)	12 (54%)	2 (15%)	
ECOG				0.257
0-1	30 (86%)	18 (82%)	12 (92%)	
2-3	5 (14%)	4 (18%)	1 (8%)	
Histology				0.002
Adenocarcinoma	27 (77%)	21 (96%)	6 (46%)	
SCC	2 (6%)	0 (0%)	2 (15%)	
Adenosquamous	1 (3%)	1 (4%)	0 (0%)	
NSCLC (NOS)	5 (14%)	0 (0%)	5 (39%)	
Mutational profile				NA
EGFR	20 (57%)	20 (91%)	0	
ALK rearrangement	2 (6%)	2 (9%)	0	
RT techniques				0.712
SBRT/SRS	19 (54%)	13 (59%)	6 (46%)	
VMAT/IMRT	12 (34%)	6 (27%)	6 (46%)	
3D	4 (11%)	3 (14%)	1 (8%)	
RT dose fractionations				0.900
Median dose (IQR)	30 (25-40)	29 (20-40)	30 (25-35)	
Median no. fractions (IQR)	5 (3-5)	5 (1-5)	5 (5-5)	
No. RT sites				0.630
1	30 (86%)	18 (82%)	12 (92%)	
2	5 (14%)	4 (18%)	1 (8%)	
Sites of RT*				NA
Bones	14 (35%)	10 (38%)	4 (29%)	
Brain	12 (30%)	9 (35%)	3 (21%)	
Lungs	9 (23%)	5 (19%)	4 (29%)	
Liver	1 (2%)	1 (4%)	0	
Adrenal	2 (5%)	1 (4%)	1 (7%)	
Lymph nodes	2 (5%)	0	2 (14%)	

* Some patients had more than 1 site treated

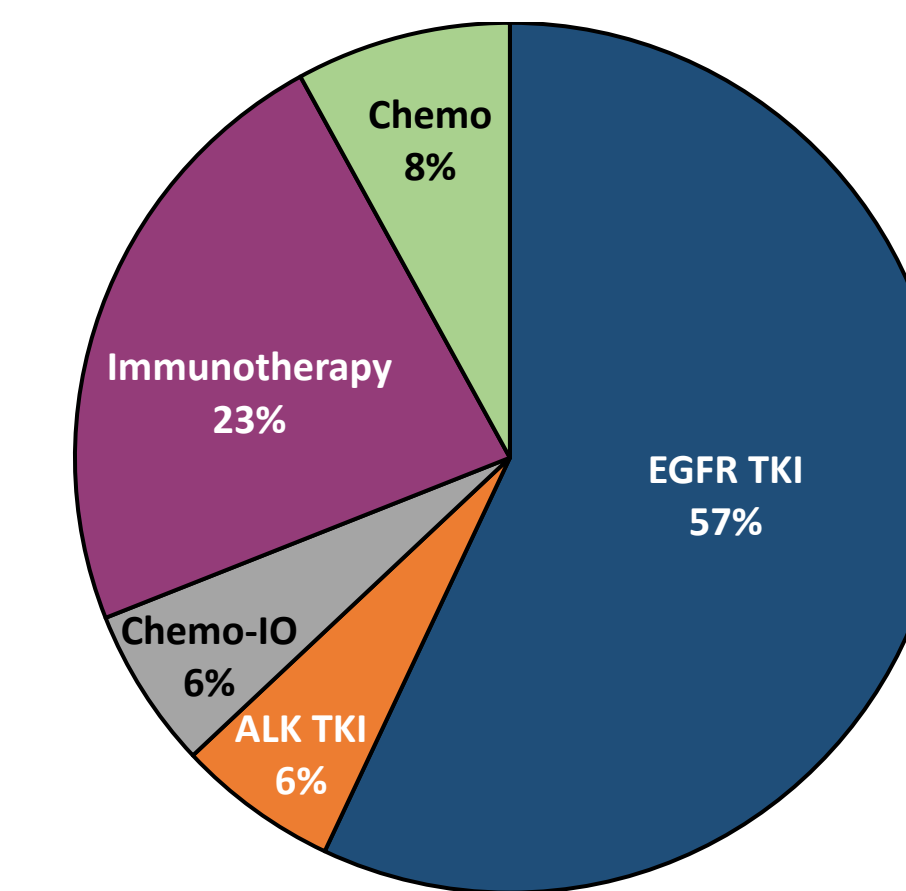


Figure 1: Types of systemic therapy that patients received at the time of oligoprogression

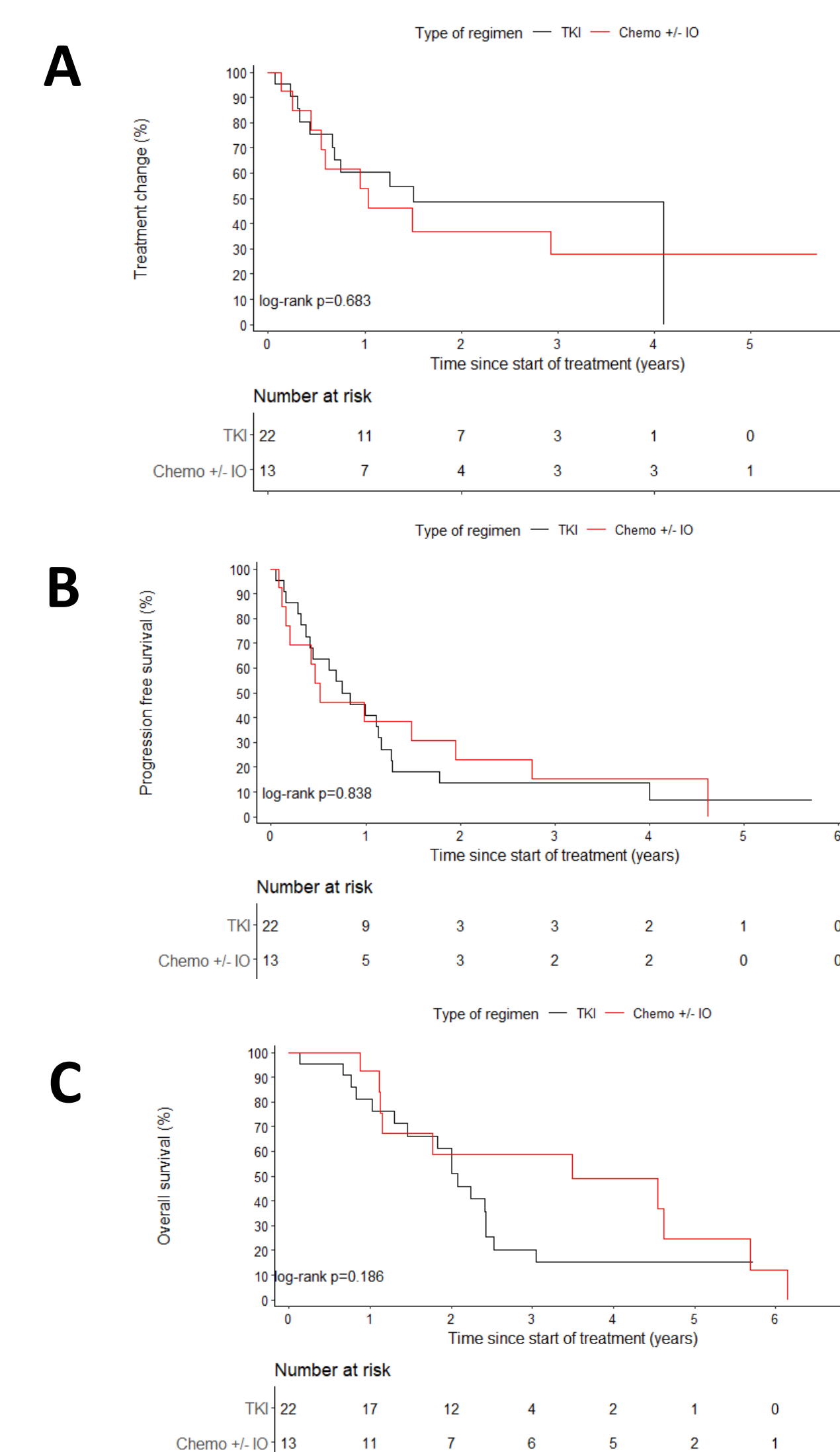


Figure 2: Kaplan-Meier plots on (A) time-to-next systemic therapy, (B) progression-free survival and (C) overall survival stratified by type of systemic therapy

DISCUSSION AND CONCLUSION

Our study showed that targeted RT to oligoprogressive sites resulted in more than half of the patients remaining on the same systemic therapy and also led to a clinically meaningful extension to the time until the next line of systemic therapy.

Our results are in keeping with the CURB trial which randomised patients with oligoprogressive breast cancer and NSCLC to SBRT and standard-of-care (SOC).¹ In the NSCLC cohort, SBRT to oligoprogressive sites increased PFS from 2 to 10 months and patients remained on the same systemic therapy longer compared to the SOC arm. In contrast, the STOP trial failed to show a significant PFS improvement after SBRT to oligoprogressive disease in patients with mixed tumour types. However, this study was affected by a high rate of patients who received ablative RT doses in the SOC arm.² Our study is limited by the small number of cases and lack of toxicity data. Nevertheless, targeted RT for oligoprogressive NSCLC enable continued use of the same systemic therapy for a clinically meaningful duration, with encouraging survival outcomes. We await the results from ongoing prospective trials such as HALT (NCT 03256981) and SUPPRESS-NSCLC (NCT 04405401).

REFERENCES & ACKNOWLEDGEMENTS

References

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