Comprehensive genomic profiling (CGP) and PD-L1 IHC in patients with advanced NSCLC: testing and treatment patterns in the real-world (RW) setting

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BACKGROUND

- In the treatment of advanced NSCLC there is increasing tension between first-line (1L) empiric combination therapy vs. precision therapy enabled by timely CGP.

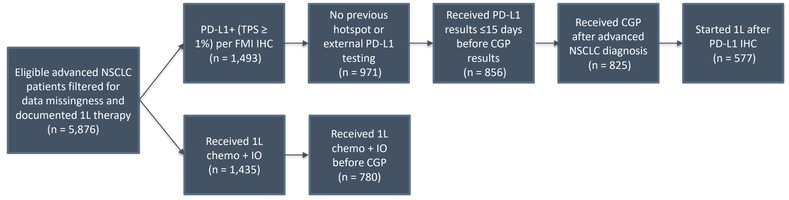
Empiric 1L Therapies	Precision 1L Therapies
Chemotherapy	Targeted CDx therapy
	Targeted Non-CDx therapy
Chemotherapy + immunotherapy	Targeted combination therapy
	Immunotherapy

- While elevated PD-L1 IHC may select for immune checkpoint inhibitor (ICI) benefit, concurrent ALK/EGFR/RET/ROS1 drivers indicate ICI resistance.
- Studying a RW advanced NSCLC clinicogenomic database (CGDB), we hypothesized that treatment prior to receipt of CGP results would enrich for chemo-based regimens (+/- ICI), while treatment after CGP would enrich for precision approaches like matched targeted therapy or ICI alone.

METHODS

Flatiron Health (FH)-Foundation Medicine (FMI) Clinico-Genomic Database (CGDB)

- This study used the nationwide (US-based) de-identified FH-FMI NSCLC CGDB. Retrospective longitudinal clinical data were derived from electronic health record (EHR) data, comprising patient-level structured and unstructured data, curated via technology-enabled abstraction, and were linked to genomic data derived from FMI CGP tests in the FH-FMI CGDB by de-identified, deterministic matching[1].
- Treatment patterns were able to be assessed for 5,876 advanced NSCLC patients diagnosed between 1/2011-12/2020.
- To study impact of CGP results, we assessed 825 advanced NSCLC patients without prior genotyping or treatment who received PD-L1 results ≤15 days prior to CGP results and studied whether treatment was initiated before or after CGP results.
- PD-L1 IHC was performed by FMI using Dako 22C3 using tumor proportion scoring (TPS). CGP was done using FoundationOne® or FoundationOne®CDx.

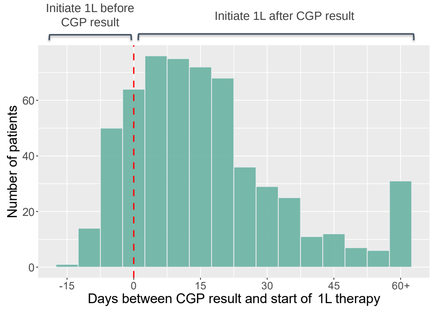


- Driver-positive patients included those that harbored ALK fusions or activating rearrangements (REs), BRAF V600E, EGFR L858R or exon 19 deletion (denoted as “EGFR canonical”), EGFR S768I, L861Q, or G719X (denoted as “EGFR rare”), KRAS G12C, MET exon 14 skipping alterations, NTRK fusions, RET fusions or activating REs, or ROS1 fusions or activating REs.

[1]Singal et al. JAMA, 2019

RESULTS

86% of patients initiate treatment after receipt of both PD-L1 IHC and CGP results

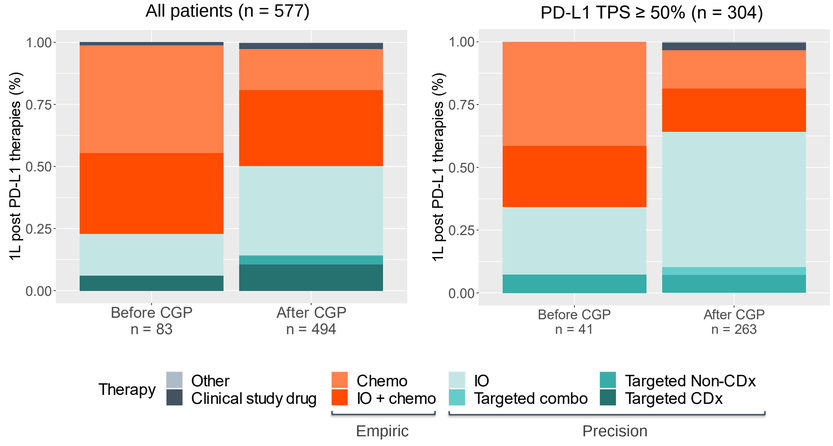


Of 825 patients who received PD-L1 IHC within 15 days of CGP results, 577 had not yet received 1L therapy at the time of PD-L1 testing.

	N
1L started before CGP	83 (14%)
1L started after CGP	494 (86%)

Of 577 previously untreated patients who received PD-L1+ IHC results before CGP results (median 7 days, range 1-15), 494 (86%) initiated 1L treatment after receipt of CGP results

50% of patients who initiate 1L treatment after CGP receive a precision therapy vs. 23% of patients who initiated treatment before CGP results

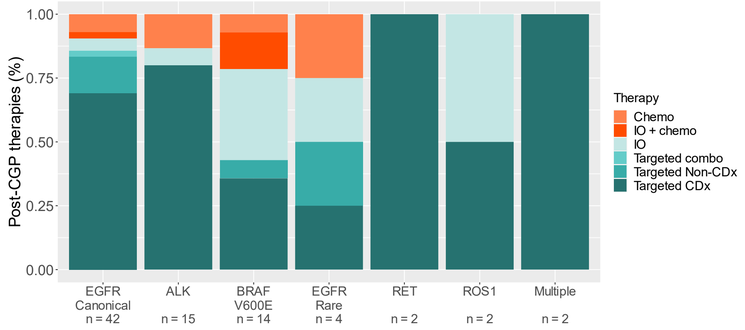


Within the PD-L1 high (TPS ≥ 50%) population, 64% of patients who initiated 1L after CGP received precision therapies (54% IO, 10% matched targeted therapy) vs. 34% of patients who initiated 1L before CGP (27% IO, 7.3% matched targeted therapy).

Disclosures: JKL, KT, AW, MC, RH, JV, GRO, and ABS are employees at Foundation Medicine, Inc. a wholly-owned subsidiary of Roche and report equity ownership in Roche.

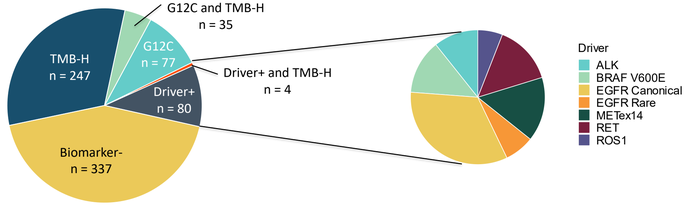
RESULTS

Of 81 patients with a guideline-recommended driver who initiated 1L after CGP, 61 (75%) received a matched targeted therapy



Of the 20 patients who did not receive 1L matched targeted therapy, 2L+ were available for 7. All 7 received matched targeted therapy in later lines.

Of 780 patients who received 1L chemo + IO prior to CGP, 286 (37%) had high TMB, 112 (14%) had KRAS G12C, and 84 (11%) had a driver detected on their CGP report which could have enabled 1L targeted therapy



CONCLUSIONS

- In advanced NSCLC patients with ≥1% PD-L1 IHC undergoing CGP, the majority of patients do not initiate therapy based on PD-L1 results only but wait until receipt of CGP results.
- In the minority of patients who initiate therapy before CGP results, chemo-based therapy is more common (76%), while precision therapies are enriched for patients who start treatment after CGP results (50%).
- 75% of patients with CGP positive for a guideline-recommended driver received matched targeted therapy following CGP, highlighting the need for further education to fully enable actionability.
- 11% of patients who received 1L chemo + IO had a targetable driver detected on a subsequent CGP report. Timely receipt of CGP results can help maximize access to precision therapies.