Poster Code: HSD42

Performance assessment of a disease-agnostic treatment sequencing heuristic for deriving line of therapy (LOT) in a real-world, rare, multi-tumor cohort across tumor mutational burden (TMB) status

Lilia Bouzit[1], Mounika Burugupalli[1], Tamara Snow[1,2], Brendan Kerr[1], Neyha Shankar[1], Kevin Andrus[1], Anosheh Afghahi[1], Cheryl Cho-Phan[1]

[1] Flatiron Health, New York, NY; [2] Now with Biograph, San Mateo, CA

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Background

- A challenge in performing retrospective observational studies using treatment data is deriving clinically appropriate treatment sequences, especially when working across cancer types.
- The objective of this study is to assess the performance of a disease-agnostic treatment sequencing heuristic for deriving LOT in a biomarker-defined, pan-tumor cohort.

Methods

- **Data source:** The US nationwide electronic health record (EHR)-derived, de-identified Flatiron Health-Foundation Medicine Enhanced Pan-tumor Clinico-genomic Database, comprising retrospective longitudinal patient-level structured and unstructured data linked to genomic data, originating from ~280 cancer clinics (~800 sites of care).
- **Inclusion criteria:** Patients diagnosed with metastatic[1] disease across 17 rare solid tumor types, known TMB status by comprehensive genomic profiling, and ≥2 LOTs were selected. Data cutoff date: 30 June 2023.
- The disease-agnostic heuristic for deriving LOT was applied to patient-level systemic, non-oral antineoplastic treatment data recorded in the EHR record and chart-abstracted oral therapy.
- Lines were evaluated by cancer, indexed to metastatic[2] diagnosis date.
- Treatment sequencing, visualization of sequencing and qualitative assessment of LOT compared to National Comprehensive Cancer Network (NCCN) preferred/recommended regimens was performed with patients stratified based on TMB-high (TMB-H) [≥10 mutations/megabase (mut/Mb)] versus non-TMB-H status (<10mut/Mb).
- Patterns of immune checkpoint inhibitor (ICI) use across cancer types were also evaluated by characterizing ICI prevalence, sequencing, and mono-/combo-ICI use among the TMB-H and non-TMB-H sub-cohorts.
- **Statistical Methods**: Descriptive statistics were summarized using N (%) and median (IQR).

Results

- Participants: 4,301 patients met eligibility criteria (Figure 1).
- Clinically appropriate LOTs and sequencing of LOTs were represented in a consistent manner across cancer types and aligned with NCCN preferred/recommended regimens.
- For patients with TMB-H tumors, ICI-therapy was well represented across most diseases with sequencing consistent with tumor-specific and tumor-agnostic approved indications for ICI-therapy (Figures 2 and 3).

[1] Patients diagnosed with Glioma were not required to have metastatic disease.
[2] Patients diagnosed with Glioma were indexed to initial diagnosis date.

Figure 1. Cohort Selection

All patients in the FH-FMI Pan-tumor CGDB at time of data cutoff date
31,084
▶ All patients in the FH-FMI Pan-Tumor CGDB with a solid tumor of interest
16,404
▶ Patients with matching FMI specimen tumor type
14,241
▶ Patients with metastatic[1] disease
11,009
▶ Patients with at least 2 LOTs
4,982
▶ Patients with TMB status available
4,301

Table 1. Patient Characteristics

Characteristic	TMB-H N = 402	non-TMB-H N = 3,899
Age, Median (IQR)	64 (55, 72)	60 (49, 68)
Gender, No. (%)		
Female	197 (49)	2,122 (54)
Male	205 (51)	1,777 (46)
Race, No. (%)		
Black/African American	18 (4.5)	304 (7.8)
Other Race	62 (15)	623 (16)
White	301 (75)	2,746 (70)
Unknown	21 (5.2)	226 (5.8)
Seen at Academic Practice, No. (%)	128 (32)	1,528 (39)
Hispanic or Latino, No. (%)	14 (3.5)	230 (5.9)
Group Stage, No. (%)		
Stage I-II	33 (8.2)	347 (8.9)
Stage III	33 (8.2)	309 (7.9)
Stage IV	221 (55)	1,759 (45)
Unknown	115 (29)	1,484 (38)
MSI-High, No. (%)	45 (12)	5 (0.1)

Table 2. Distribution of Patient Count by Tumor Type and Stratified by TMB Status

Cancer Type (total patients), No. (%)	TMB-H	non-TMB-H
1. Adrenal Cortical Carcinoma (34)	6 (18)	28 (82)
2. Anal Carcinoma (129)	22 (17)	107 (83)
3. Appendiceal Carcinoma (123)	8 (7)	115 (93)
4. Biliary Tract Carcinoma (BTC)* (675)	38 (6)	637 (94)
5. Small Intestine Carcinoma (133)	14 (11)	119 (89)
6. Cervical Carcinoma* (215)	46 (21)	169 (79)
7. Cutaneous Squamous Cell Carcinoma* (53)	39 (74)	14 (26)
8. Merkel Cell Carcinoma* (57)	23 (40)	34 (60)
9. Thyroid Carcinoma (Anaplastic, Papillary/Follicular) (104)	6 (6)	98 (94)
10. Glioblastoma Multiforme (GBM) (693)	26 (4)	667 (96)
11. Non GBM Glioma (201)	6 (3)	195 (97)
12. Non Cutaneous Melanoma* (110)	5 (5)	105 (95)
13. Gastrointestinal Neuroendocrine Tumor (non-pancreatic) (207)	9 (4)	198 (96)
14. Lung Neuroendocrine (134)	24 (18)	110 (82)
15. Pancreatic Neuroendocrine Tumor (182)	14 (8)	168 (92)
16. Occult/Unknown Primary (377)	88 (23)	289 (77)
17. Soft Tissue Sarcoma** (874)	28 (3)	846 (97)

* denotes tumor type in which ≥1 checkpoint-inhibitor therapies have received tumor-specific FDA-approval
** ≥1 checkpoint-inhibitor therapies have received FDA-approval for the subset of patients with alveolar soft part sarcoma

Figure 2. Assessment of ICI use by TMB status, Line Number

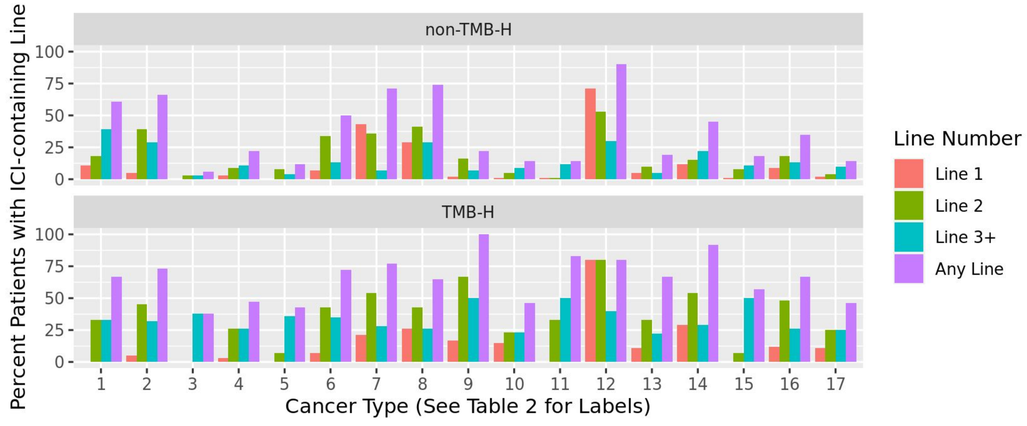
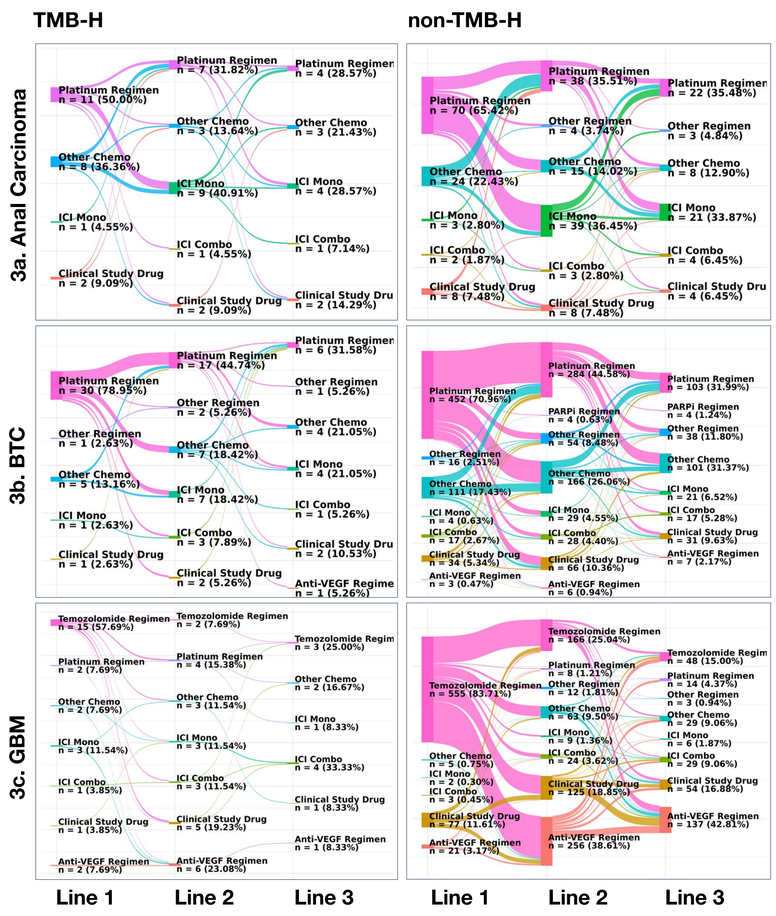


Figure 3. Sankey Diagrams, Select Cancer Types



Conclusions

- A disease-agnostic treatment sequencing heuristic for deriving LOT is feasible and can define clinically appropriate LOTs across a pan-tumor patient cohort.
- Performance was confirmed by assessing exposure to ICI-therapy stratified by TMB status.
- This approach may be applied to other real-world disease-agnostic datasets to facilitate treatment-related analyses.

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Author Contact Info: Lilia Bouzit, lilia.bouzit@flatiron.com