A Precision Oncology Approach to Geriatric Cancer Care: Real-World Experience with Comprehensive Genomic Profiling and Clinical Outcomes

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Background:
Older adults with cancer are clinically heterogeneous, with varying degrees of frailty, comorbidity, and treatment tolerance. Although potentially actionable genomic alterations are present in this population, geriatric patients remain under-represented in precision oncology evidence. In real-world geriatric oncology practice, the clinical utility of comprehensive genomic profiling (CGP) and its impact on patient outcomes remain poorly characterized. We evaluated real-world CGP utilisation, clinical utility, and outcomes in geriatric patients with solid tumors managed in our Precision Oncology Clinic.

Methodology:
We conducted a retrospective observational study of 563 older adults (≥65 years) with solid malignancies. Based on the availability and performance of comprehensive genomic profiling (CGP) as part of routine clinical care, patients were classified into two cohorts: Cohort A (CGP

cohort), who underwent CGP testing, and Cohort B (non-CGP cohort), patients in whom CGP testing was not performed. Clinical demographics, molecular landscape, treatment received, and outcome data were collected from medical records. Geriatric status was assessed using ECOG performance and the Charlson Comorbidity Index (CCI), and patients were categorised as fit, intermediate, or frail. In Cohort A, CGP findings were evaluated for clinically actionable genomic alterations in various cancer subtypes. Treatment response at 3 months and progression-free survival (PFS) were assessed from available clinical and radiological records for both the cohorts.

Results

Among 563 older adults evaluated at the Precision Oncology Clinic, the median age was 70 years in Cohort A and 72 years in Cohort B; overall, 324 (57.5%) patients were male and 239 (42.5%) were female. Gastrointestinal and thoracic malignancies were the predominant tumour groups. Patients were divided on the basis of the availability of genomic report in two group: cohort A (CGP cohort) and cohort B (non-CGP Cohort). 405 (71.9%) comprised cohort A (CGP cohort), while 158 (28.1%) comprised cohort B (non-CGP cohort). Geriatric assessment incorporating ECOG performance status and Charlson Comorbidity Index (CCI) categorised patients as fit, intermediate, or frail. In Cohort A, 189 (46.7%) patients were fit, 143 (35.3%) were intermediate, and 73 (18.0%) were frail, compared with 80 (50.6%), 35 (22.2%), and 43 (27.2%), respectively, in Cohort B.

CGP identified clinically actionable genomic alterations in 294/405 (72.6%) patients in Cohort A. TP53 (35%), EGFR (20%), PIK3CA (16%), KRAS (12%), ERBB2 (9%), and BRAF (7%) were the most frequently altered genes, with EGFR (n=64) alterations occurring predominantly in thoracic malignancies, PIK3CA (n=21) and ERBB2 (n=9) alterations predominantly in breast and gynaecological malignancies, KRAS (n=34) alterations primarily in thoracic and gastrointestinal malignancies, and BRAF (n=7) alterations distributed across thoracic, gynaecological, and CUP tumours. In addition, CGP identified immunotherapy-relevant biomarkers, including a high TMB-positive PD-L1 score (more than 1) (n=14), and MSI-H status (n=6), enabling biomarker-guided immunotherapy in selected patients. The median number of prior systemic therapies was 2 in both cohorts.

In the CGP Cohort , 221 patients received precision-guided treatment, 111 received standard care, 16 received best supportive care and 57 were lost to follow-up; in the Non-CGP Cohort, 134 received standard clinical care and 24 received best supportive care. At 3 months, among response-evaluable patients, the CGP Cohort demonstrated 18 complete responses (CR), 139 partial responses (PR), 87 stable disease (SD), and 74 progressive disease (PD), compared with 2 CR, 71 PR, 45 SD, and 9 PD in the non-CGP cohort. Median PFS was 6.8 months in the CGP cohort and 2.6 months in the non-CGP cohort, with PFS assessed independently within each cohort, which was statistically significant.

Conclusion:

Comprehensive genomic profiling demonstrated meaningful clinical utility in geriatric oncology, with actionable genomic and biomarker findings translated into individualised treatment across a clinically heterogeneous older population. Importantly, treatment translation extended to patients with varying degrees of frailty and comorbidity, suggesting that geriatric vulnerability should not, by itself, preclude consideration of precision oncology. Integrating genomic profiling with geriatric assessment may enable biologically informed, individualised cancer care for older adults.