Abstract 4124 : Molecular profile of hepatocellular carcinoma (HCC) in older (OA) versus younger adults (YA) receiving tyrosine kinase inhibitors: does age matter?

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Background

- HCC is associated with significant geriatric comorbidities, with the median age of diagnosis being 65 years.
- Further, multi-kinase inhibitors (MKIs) are associated with up to 60% of grade 3-4 toxicities.
- While not an independent risk factor, age significantly influences patient outcomes.
- We aim to analyze the association of survival with age in HCC and identify molecular markers associated with survival in older patients with HCC receiving TKIs.

Methods

- 1473 HCC specimens with DNA/RNA sequencing were profiled at Caris Life Sciences.
- The study cohort was stratified based on median age at specimen collection into two groups: OA: age>65 and YA: age<=65.
- Real-world overall survival (OS) data was obtained from insurance claims and Kaplan–Meier estimates of OS were calculated from specimen collection to last clinical contact; and MKI time on treatment (TOT) from the initiation to termination of treatment.
- Hazard ratios (HR) and p-values were calculated using the Cox proportional hazards model and the log-rank test, respectively.

Results

Table 1. Patient Demographics

Patient Demographics		OA (n=757)	YA (n=716)	q-value
Age				
	Median Age [range] (N)	73.0 [66.0 - 90.0] (757)	60.0 [12.0 - 65.0] (716)	<0.001
Gender				
	Male	75.8% (574/757)	76.3% (546/716)	0.919
	Female	24.2% (183/757)	23.7% (170/716)	
Smoking History				
	Smoker	9.9% (75/757)	9.2% (66/716)	0.814
	Non-smoker	1.1% (8/757)	1.7% (12/716)	
	Smoking History Unknown	89.0% (674/757)	89.1% (638/716)	
Race				
	White	68.4% (518/757)	45.1% (323/716)	<0.001
	Black or African American	13.2% (100/757)	13.7% (98/716)	
	Asian or Pacific Islander	4.5% (34/757)	5.7% (41/716)	
	Other	4.0% (30/757)	5.3% (38/716)	
	Race Unknown	9.9% (75/757)	30.2% (216/716)	
Ethnicity				
	Not Hispanic or Latino	77.7% (588/757)	55.4% (397/716)	<0.001
	Hispanic or Latino	13.3% (101/757)	13.1% (94/716)	
	Ethnicity Unknown	9.0% (68/757)	31.4% (225/716)	
Specimen Site				
	Primary	72.1% (546/757)	73.0% (523/716)	0.919
	Metastatic	26.9% (204/757)	26.1% (187/716)	
	Unclear/Other	0.9% (7/757)	0.8% (6/716)	

Table 1: Patient demographics. OA population predominantly comprised of whites and not-Hispanic/Latinos, although a significant proportion of YA lacked Race/Ethnicity information. No differences in gender, smoking history or biopsy sites were noted.

Results

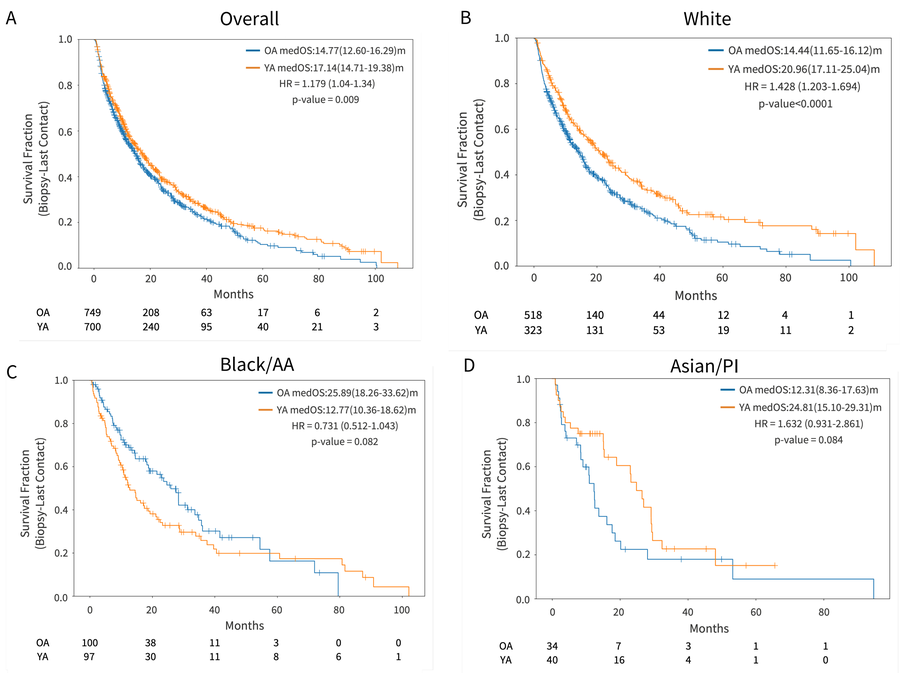

Figure 1:Association of age with OS. OA were associated with poor OS, with the survival differences more pronounced among Whites (A). Although not statistically significant, OA was associated with longer OS among Black/AA (B).

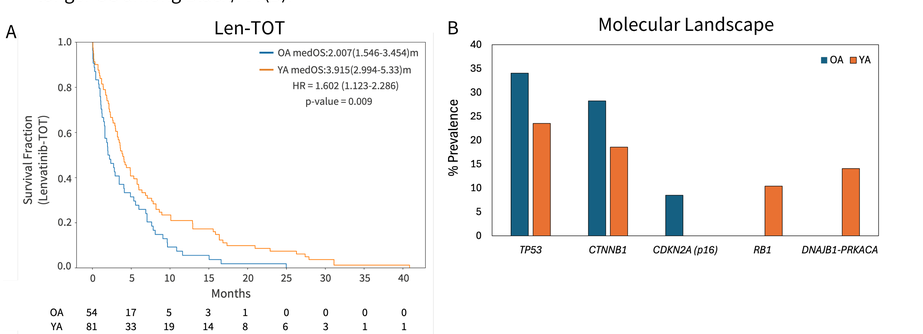

Figure 2 :Len-TOT and molecular alterations associated with age. OA were associated with a significantly shorter time on Lenvatinib treatment (A) . Although not statistically significant, OA were associated with an increased prevalence in *TP53*, *CTNNB1* and *CDKN2A* mutations while YA were associated with an increased prevalence in *RB1* mutations and *DNAJB1-PRKACA* fusions (B).Alterations with a difference in prevalence of at least 5% between the two cohorts are displayed.

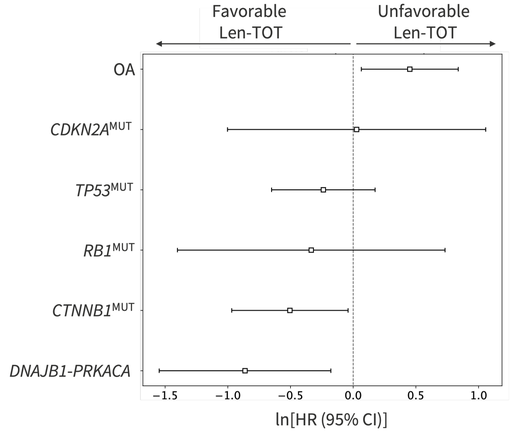

Figure 3: Multivariate analysis (MVA) of factors associated with Len-TOT.
Molecular alterations identified earlier were utilized as co-variates in the MVA. Adjusted hazard ratios (HR) and 95% confidence intervals (CI) are shown for each co-variate. OA was independently associated with longer Len-TOT (HR=1.6) while CTNNB1 mutations and DNAJB1-PRKACA fusions were associated with longer Len-TOT (HR = 0.4-0.6, all p<0.05)

Summary

- Median OS (mOS) among OA was 14.8 months(m) vs 17.1m among YA (HR: 1.18, p<0.01)
- The difference in mOS was even more pronounced among White OA (HR:1.43, p<0.0001) and Asian/Pacific Islanders (HR:1.62, p=0.084). Interestingly, although not statistically significant, OA was associated with longer mOS in Black/African Americans (HR:0.73, p=0.082)
- OA was not associated with MKI-TOT such as sorafenib or cabozantinib. However, OA was associated with a shorter TOT (HR 1.6, p<0.01) on Lenvatinib
- MVA revealed that OA was independently associated with shorter Len-TOT (HR 1.6, p 0.01), while *CTNNB1* mutations and *DNAJB1-PRKACA* fusions were independently associated with longer Len-TOT (HR 0.4-0.6, both p<0.05).

Conclusion

- OA was associated with differing survival trends between whites and Asian/PI compared to Black/AA. Further, OA was associated with shorter Len-TOT, potentially due to anti-angiogenic toxicity.
- Our limitations include an inability to investigate race-based differences on Len-TOT due to small sample sizes (Black/AA: n=18, Asian/PI: n=15) and the lack of toxicity and geriatric assessment data.
- Future studies including race, geriatric assessments and toxicity profiles should be considered to understand survival and tolerability differences