• 2021 Jan;157:103187.
• 2021 Jan;157:103187.

Abstract #9579: Leveraging personalized circulating tumor DNA (ctDNA) for detection and monitoring of molecular residual disease in high-risk melanoma

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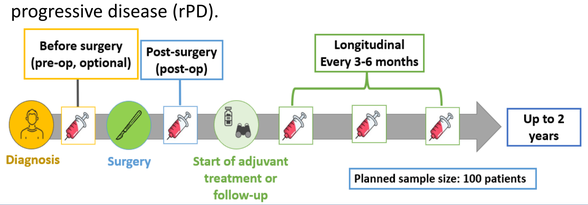
BACKGROUND

- Locally advanced melanoma has a variable prognosis [1].
- Adjuvant immuno- (IO) and targeted therapy (TT) are approved for stage III-IV resected disease [2-5]. However, a significant proportion of patients (pts) are cured by local treatment alone or relapse despite adjuvant therapy.
- Liquid biopsy has been used to predict benefit from systemic therapy and identify pts at higher risk of disease relapse and death [6].
- Personalized ctDNA assays are a highly sensitive approach that may enhance upfront risk stratification and early detection of relapse [6].

METHODS

- Serial ctDNA Monitoring as a predictive Biomarker in advanced neoplAsms (SAMBA) is a Princess Margaret initiative (NCT03702309) evaluating ctDNA kinetics in longitudinal samples collected from high-risk melanoma pts.
- Personalized amplicon based NGS assays by Inivata (RaDaR®) were used to detect somatic variants in ctDNA identified through whole-exome sequencing of matched tumor tissue [7-8].
- Progression free survival (PFS) and overall survival (OS) from the time of surgery were estimated with the Kaplan Meier analysis and compared with the log-rank test.

Figure 1: Study schema. Samples are collected from pts with stage IIB-IV resected melanoma, who post-surgery, undergo regular surveillance follow-up or adjuvant systemic treatment with either IO or TT. Plasma is collected pre-op (if feasible), post-op (after surgery), and every 3-6 months (m) around the time of radiological restaging, until radiological progressive disease (rPD).



RESULTS

Total N of patients	**53**
Age (median)	66 (27-87)
Follow-up (median)	27 mo (6-45)
Gender	
Female	17 (32%)
Male	36 (68%)
Stage	
II	7 (13%)
III	35 (66%)
IV	11 (21%)
BRAF	
Mutated	23 (43%)
Wild Type	30 (57%)
Adjuvant Systemic Therapy	
None	13 (25%)
Immunotherapy	30 (57%)
Targeted therapy	7 (13%)
Unknown (clinical trial)	3 (5%)
Adjuvant Radiation	
Yes	12 (23%)
No	41 (77%)
Progressive Disease	
Yes	16 (30%)
No	37 (70%)

Table 1: Clinical characteristics of 53 pts with stage IIB-IV melanoma, treated with surgery followed by surveillance follow up or adjuvant systemic therapy.

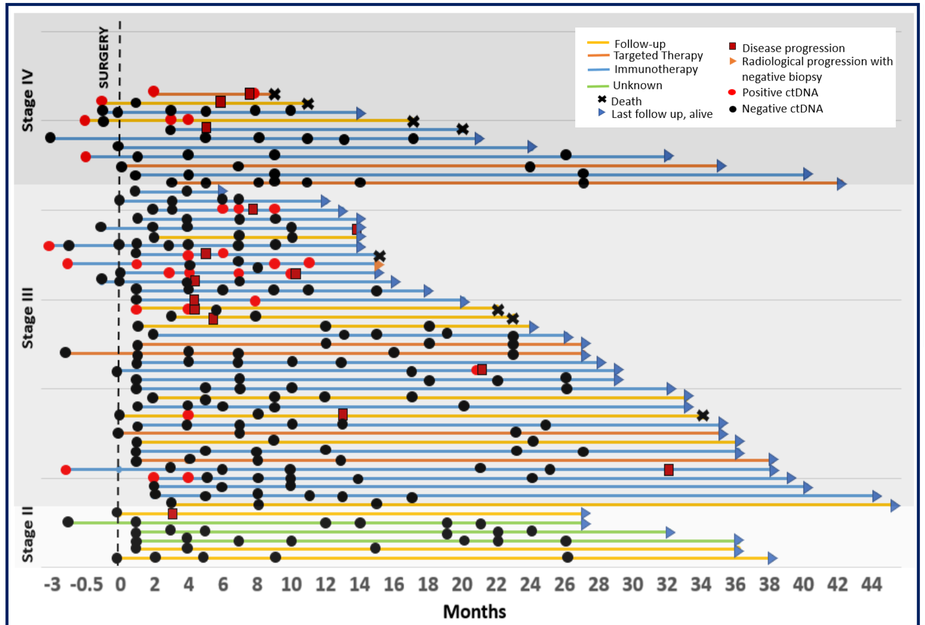


Figure 2: Change in ctDNA detectability during adjuvant treatment and survival follow-up (N= 53 patients). Patients are stratified according to disease stage and treatment received after surgery. The length of each line correspond to the duration of survival from the time of surgery to death or last follow-up. A square symbol indicates rPD. ctDNA+ and ctDNA- collections are indicated with red and black circles, respectively. Three pts with rising ctDNA over time experienced rPD after a median of 4 m (2-7).

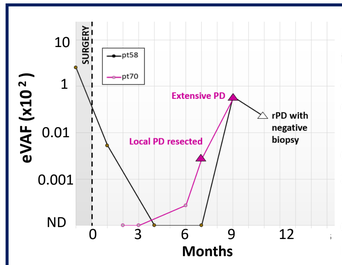


Figure 4: Examples of ctDNA changes in two pts with stage III disease receiving adjuvant IO and their correlation with clinical outcomes. Pt 58 had pre-op and post-op ctDNA+, cleared after the start of IO. At 8m the pt had a rise in ctDNA associated with rPD with negative biopsy. The pt continued IO with decrease of ctDNA and of the disease on radiological imaging.

Pt 70 had post-op ctDNA– which become positive at 6 m predicting a local recurrence. The patient had surgical resection of the recurrent disease. Despite this, developed further PD associated with further rise of ctDNA.

	Pre-op		Post-op		Longitudinal		at PD
	PD	Non-PD	PD	Non-PD	PD	Non-PD	
ctDNA+	3 (60%)	3 (43%)	3 (19%)	2 (6%)	11 (41%)	2 (1%)	7 (87%)
ctDNA-	2 (40%)	4 (57%)	13 (81%)	33 (94%)	16 (59%)	132 (99%)	1 (13%)
Total	5	7	16	35	27	134	8

Table 1: ctDNA+ and ctDNA- samples collected before surgery (pre-op), after surgery (post-op) and at subsequent time points from all the participants, according with clinical outcome.

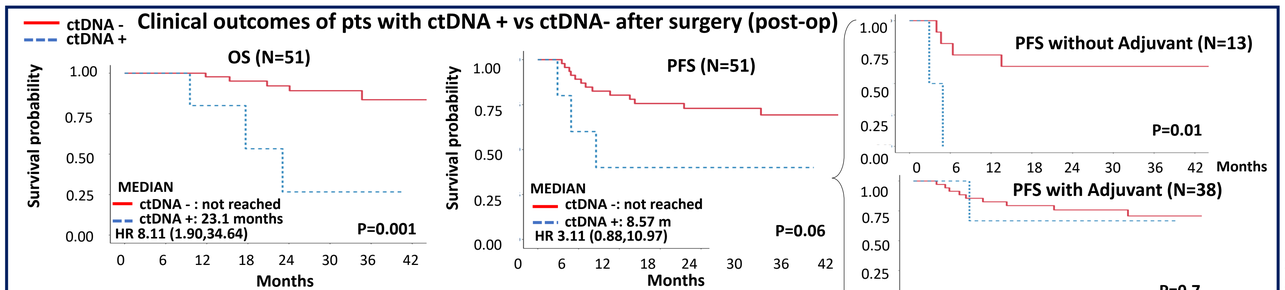


Figure 3: OS and PFS in patients with ctDNA+ vs ctDNA- at the first collection post surgery (post-op). Post-op collection within 3 m was available for 51/53 pts (96%).

We observed a significant prolongation of median OS in patients with ctDNA - in this population. No significant difference was observed in terms of PFS for the overall population based on post-op ctDNA detectability. However, in patients not receiving adjuvant treatment ctDNA+ at post-op collection was associated with shorter PFS. No differences were observed in patients with ctDNA+ vs ctDNA– in samples collected before surgery (data not shown).

CONCLUSIONS

- Personalized ctDNA analysis with RaDaR® may improve risk of death stratification and selection of pts who could benefit from adjuvant treatment.
- Detection of ctDNA may precede rPD.
- Follow-up will continue in pts with rising ctDNA who have not yet had rPD.
- Pts accrual and sample collection are ongoing.

AKNOWLEDGMENT

This study is performed under the auspice of the LIBERATE study, supported by the BMO Chair in Precision Cancer Genomics. The following grants and awards have also contributed to supporting this study: Douglas Wright Melanoma Award, Division of Medical Oncology and Hematology Young Investigator Award, Catalyst and Invest in Research Princess Margaret grants.
We thank all patients and their families who participated in the study.

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