Abstract: S246

Title: CLINICAL IMPLICATIONS OF CTDNA IN RESIDUAL DISEASE ASSESSMENT, PROGNOSIS PREDICTION, DISEASE MONITORING FOR NEWLY PERIPHERAL T-CELL LYMPHOMA PATIENTS

Abstract Type: Oral Presentation

Session Title: T cell lymphoma from biology to clinic

Background:

Pretreatment circulating tumor DNA (ctDNA) (Pre-ctDNA) burden has been reported as a surrogate for tumor burden with prognostic information in lymphomas including peripheral T cell lymphomas (PTCLs). Furthermore, it is important to know whether first-line CHOP-like regimens fail to achieve minimal residual disease (MRD) negativity of the end-of-treatment (EOT) detected by ctDNA is the true culprit for the high incidence of relapse for PTCL patients.

Aims:

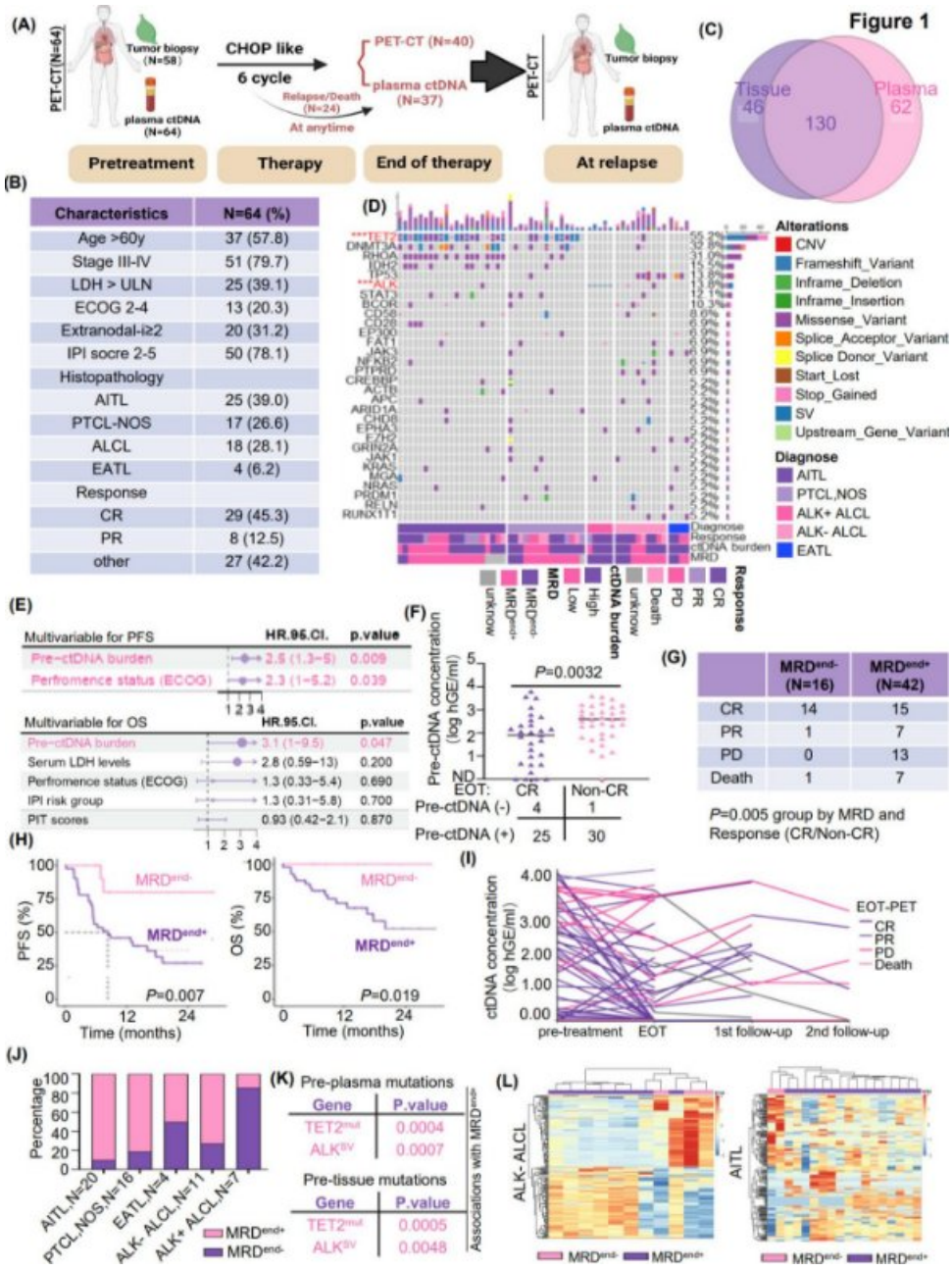
This study aimed to evaluate the utility of dynamic plasma ctDNA to residual disease assessment, prognosis prediction, and disease monitoring in patients with PTCLs.

Methods:

Here, using a 475 gene lymphoma-specific sequencing panel, we assessed the prognostic and predictive utilities of ctDNA measurements before, during, and after first-line therapy in 64 Chinese PTCL patients, the detailed sample collection and radiological imaging were shown in **Figure 1A**. By the last visit in 01 Jan 2024, the median follow-up duration was 22.3 (range, 10.2−36.1) months. All patients received CHOP-like regimens.

Results:

The clinical characteristics of the 64 patients were shown in**Figure 1B**. The top 30 somatic mutations of tissue samples were shown in **Figure 1D**. Pre-ctDNA achieved an overall sensitivity of 73.9%% (130/176) in detecting variants verified in tumor, indicating that ctDNA is a reliable source for PTCL genotyping. In addition, ctDNA allowed for the identification of an additional 62 somatic mutations that were undetectable in tumor genomic DNA (gDNA), which demonstrated that ctDNA could overcome tumor spatial heterogeneity (**Figure 1C**). Pre-ctDNA burden was significantly associated with clinical characteristics, including extranodal involvement (*P*=0.009), lactate dehydrogenase (LDH) levels (*P*=0.015), stage (*P*=0.011), bone marrow involvement (*P*=0.019) and IPI score (*P*=0.015). As regards to the histopathology of PTCL, pre-ctDNA burden was significantly high in angioimmunoblastic T-cell lymphoma (AITL) compared with other subtypes (*P*=0.035). High ctDNA burden determined a worse prognosis independently of conventional risk factors (**Figure 1E**). A significant difference of pre-ctDNA burden existed between complete remission (CR) and non-CR group, and pre-ctDNA negative group presented with higher CR rate at the EOT (**Figure 1F**). Among the 37 patients who can achieved partial remission (PR) / CR by PET-CT, only 15 patients (40.5%) can achieve MRD negative (MRDend-) (*P*=0.005, **Figure 1G**). Furthermore, MRDend- group was associated with higher remission rate. At the EOT response evaluation, ctDNA was detected in 72.4% (42 of 58, MRD positive, MRDend+) of the patients with extremely poor outcomes (**Figure 1H**), and primary refractory diseases were characterized by high ctDNA burden at EOT (**Figure 1I**). Next, we explored the clinical and biological factors associated with MRDend+ in different subtypes of PTCL. As regard to the histopathology of PTCL, only ALK+ anaplastic large cell lymphoma (ALCL) patients can achieve a higher proportion of MRDend- (**Figure 1J**). Furthermore, MRDend+ was significantly associated with clinical characteristics of age>60y (*P*=0.036) and high pre-ctDNA burdens (*P*=0.014). MRDend- was significantly positively associated with pretreatment ALK-rearrangement and negatively associated with pretreatment TET2-mutation both in tissue and plasma (**Figure 1K**). Different GEPs were observed between MRDend- and MRDend+ patients in ALK- ALCL and AITL (**Figure 1I**).



Summary/Conclusion:

ctDNA is a promising noninvasive tool for prognosis prediction, residual disease assessment, and disease monitoring for newly diagnosed PTCL patients.

Keywords: ctDNA, MRD, CHOP, Peripheral T-cell lymphoma