

Introduction

Circulating tumour DNA (ctDNA) has been studied in several articles in recent years for its potential use in clinical practice as a prognostic biomarker for melanoma patients. Here, we present the results of a systematic literature review and meta-analysis of the available evidence on the association between ctDNA levels and survival of melanoma patients.

Methods and Materials

We searched studies published until December 2019 in MEDLINE and EMBASE. We used random effects meta-analysis models to calculate summary hazard ratio (SHR) and 95% confidence intervals (CI) for the association between ctDNA (measured before any treatment was started or in the follow-up) and the survival of melanoma patients, and quantified the between-estimates heterogeneity using the I² statistics.

Results

We included 26 studies published between 2009 and 2019 for over 2,000 melanoma patients: mostly stage III-IV. BRAF-mutant ctDNA was searched in most studies, while somatic mutations of other genes were searched in the minority of studies. Melanoma patients with detectable ctDNA before treatment had worse progression-free survival (PFS) (SHR 2.47, 95%CI 1.85-3.29, Fig 1) and overall survival (OS) (SHR 2.98, 95%CI 2.26-3.92, Fig 2) compared to patients with undetectable ctDNA, with no significant difference by tumour stage. ctDNA detectability during follow-up was also associated with poorer patients' PFS (SHR 4.27, 95%CI 2.75-6.63; fig 3) and OS (SHR 3.91, 95%CI 1.97-7.78, Fig. 4); in the latter case, association of ctDNA with outcome was stronger (p=0.01) for stage IV vs. III melanomas. Between-estimates heterogeneity was low for all pooled estimates.

Conclusion

ctDNA is a strong prognostic biomarker for advanced-stage cutaneous melanoma patients, robust across a wide range of tumour (e.g. genomic profile) and patients (e.g. systemic therapy) characteristics.

Flow-chart of the selection process for the studies included in the literature review and meta-analysis on the association between circulating tumour DNA and survival of melanoma patients.

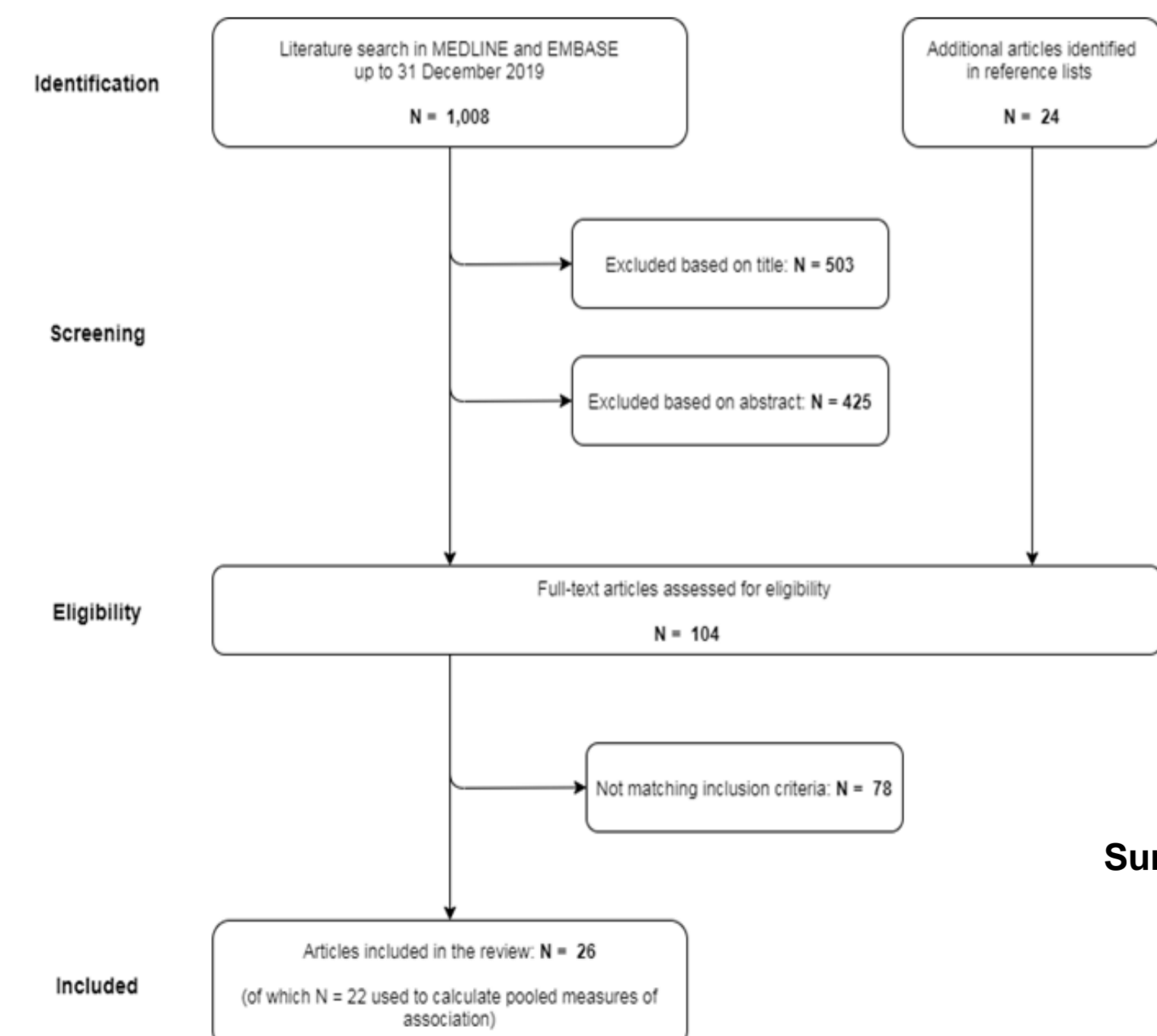


Fig. 1. Forest plot for the association between ctDNA levels measured before treatment and progression-free survival of melanoma patients.

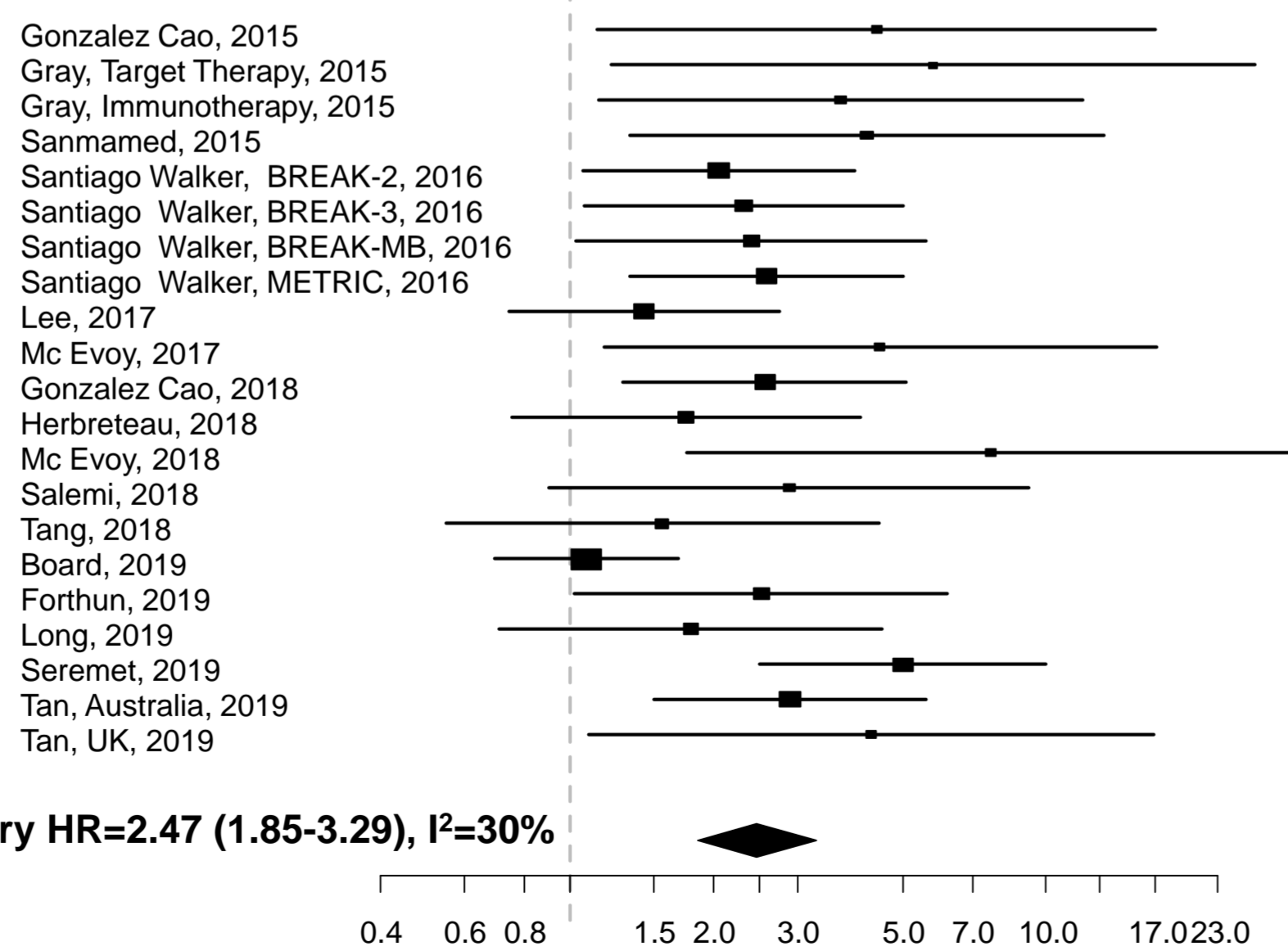


Fig. 2 Forest plot for the association between ctDNA levels measured before treatment and overall survival of melanoma patients

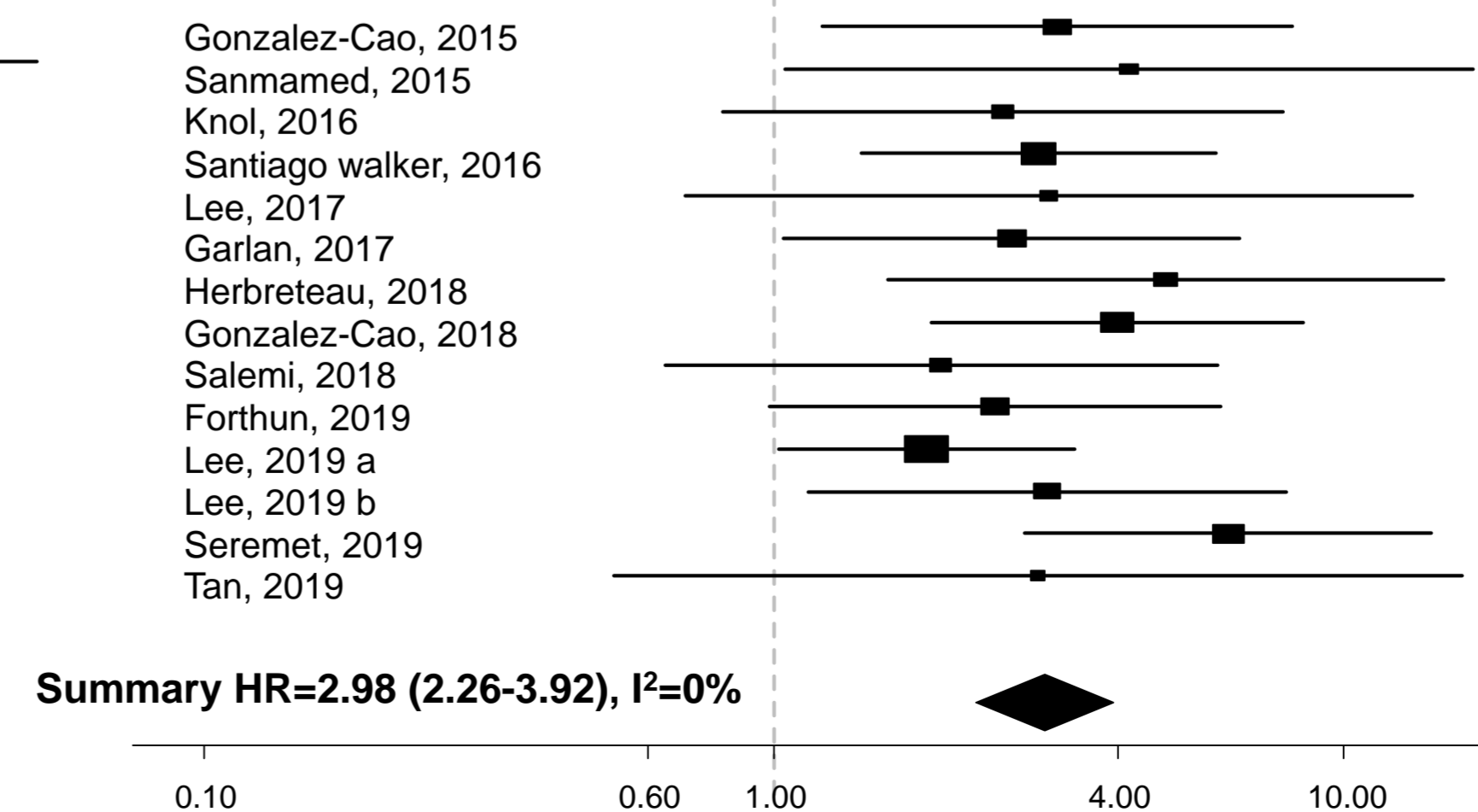


Fig. 3 Forest plot for the association between ctDNA levels measured during treatment and progression-free survival of melanoma patients.

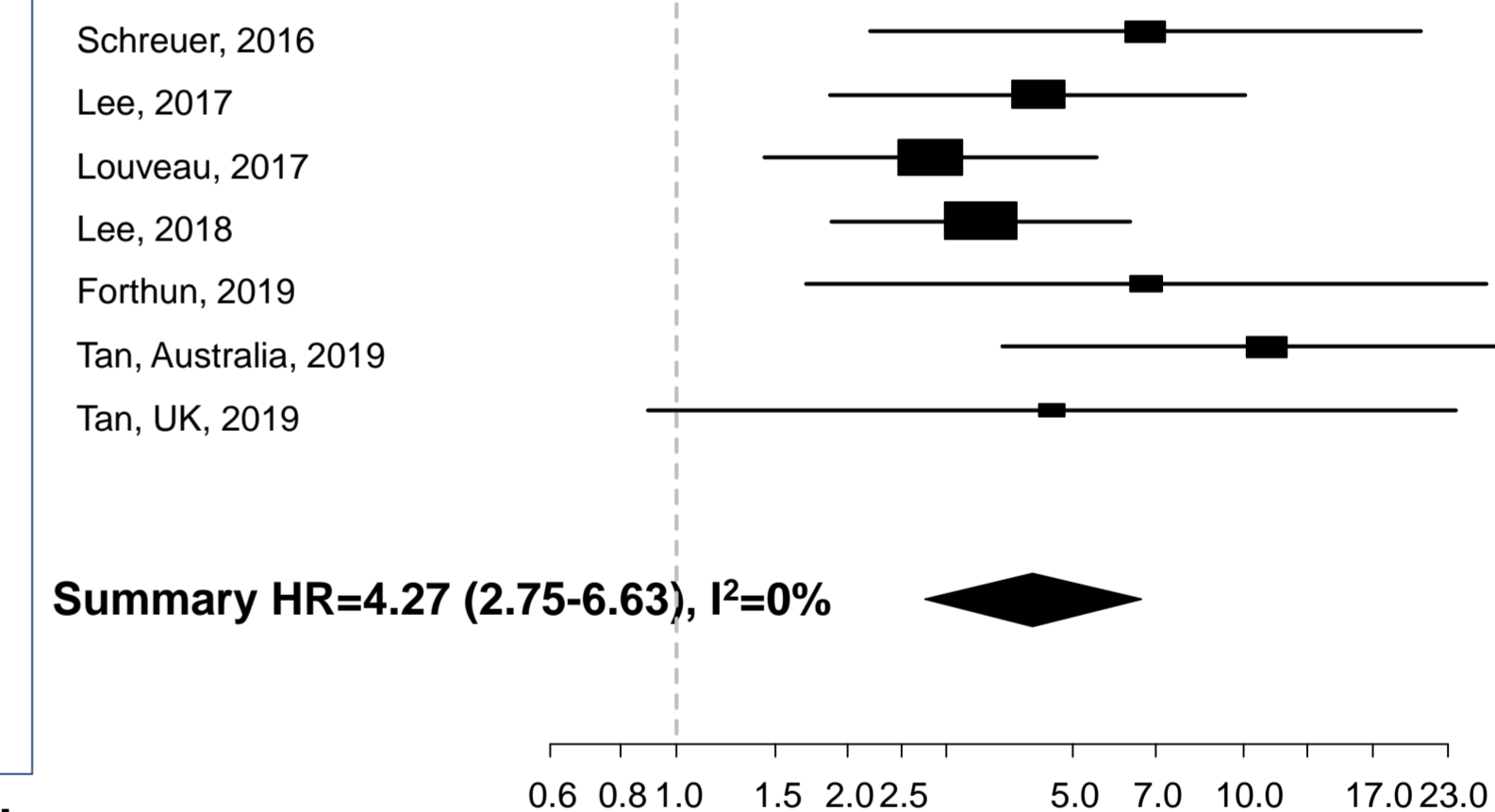


Fig. 4 Forest plot for the association between ctDNA levels measured during treatment and overall survival of melanoma patients.

