Baseline chemotherapeutic strategies in non-small cell lung cancer (NSCLC) patients and are reduced by platinum-based chemotherapy (PCT) and ICI combinations.

Roberto Ferrara 1,2, Giuseppe Lo Russo 3, Chiara Maura Ciniselli 2, Stefano Di Gregorio 1, Giuseppina Calaneso 1, Barbara Bassani 1, Claudia Proto 1, Arselà Preila 1, Marianna Mambrelli 1, Alessandro De Toma 1, Mario Occhipinti 1, Sara Mangiaviti 1, Teresa Beninato 1, Laura Mazzocco 1, Monica Ganzinelli 1, Filippo da Braud 1, Marina Chiarà Garasian 1, Mario Paolo Colombò 1, Paolo Verderio 1, Sabina Sangaletti 2

1 Department of Medical Oncology, Istituto Nazionale dei Tumori, Milano, Italy, 2 Molecular Immunology Unit, Istituto Nazionale dei Tumori, Milano, Italy, 3 Bioinformatics and Biostatistics Unit, Istituto Nazionale dei Tumori, Milano, Italy

Methods: NSCLC pts treated with PCT-ICI-LDNs (at baseline and during treatment) were retrospectively evaluated. In 1st line the single-agent ICI cohort (n=75) 59% had PD-L1 on tumor cells ≥50% (Table 1). Among 67 patients evaluable for response, response rate (RRR) was 34%. PD and HPD occurred in 19 (28%) and 6 (9%) pts, respectively (Fig 1). Before ICI start, HPD pts had significantly higher median percentage of circulating immature CD10- LNPIs neutrophils 48.6% (min 30.36; max 82.6) vs 76.9% (min 1.06; max 200) (p < 0.001) (Table 2). These results were confirmed by unpaired analysis of CD10 expression on circulating LDNs (Fig 3). The percentage of CD10+ immature LNPIs was identified by Youden index to discriminate HPD from others. In the PCT-ICI cohort, 10 pts had CD10- neutrophils >35% being at high HPD risk, however none of them experienced PD. 7 of these 10 HPD pts responded to ICI. HPD pts had available dynamic LDNs evaluation upon PCT-ICI treatment (Fig 4). CD10- neutrophils decreased in median -45.2% (gate CD15+) while in 6 pts with PD upon single-agent ICI, only a 2.5% decrease occurred, suggesting that PCT prevents HPD by reducing CD10- LDNs (Fig 5).

RESULTS

1st line single agent ICI

1st line chemo-ICIs combination

METHODS

RESULTS

CONCLUSIONS

Low density neutrophils influence on T-cells proliferation survival and senescence. Lower density neutrophils survival and sensitivity to cisplatin induced cell death.

Higher baseline immature CD10- LDNs is a circulating biomarker of HPD upon single agent ICI, as identified by the Youden index (25%) which supports T-cell proliferation and induce T-cell senescence.

The addition of PCT prevents HPD reducing the immature neutrophils subsets by necrotic cell death.

Higher CD10- LDNs could be a biomarker to select pts for whom adding PCT to ICI in 1st line may avoid HPD.