1048P Molecular predictors of immunotherapy efficacy in lung squamous-cell carcinoma (LSCC): Results from the randomized prospective SQUINT trial

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Abstract

Introduction: Immunotherapy as single agent or in combination is the standard of care for metastatic non-small-cell lung cancer (NSCLC), including LSCC. The SQUINT trial was a randomized, prospective, phase II trial which assesses the efficacy of nivolumab plus investigator-choice platinum-based chemotherapy (N-CT) versus the combination of nivolumab and ipilimumab (NI) in patients with advanced/metastatic LSCC. **Methods:** All eligible patients were randomly assigned to either NI or N-CT. Nivolumab was administered at the standard dose of 360 mg every 3 weeks, while ipilimumab was administered at the dose of 1 mg/kg every 6 weeks. The primary endpoint was overall survival (OS) at 12 months. Availability of an adequate tumor sample obtained before trial inclusion was mandatory. All samples were analyzed using the Vela Diagnostics' OncoKey SL 525 Plus Panel that is a next-generation sequencing (NGS) assay that enables comprehensive genomic profiling of tumor samples. The panel contains 525 cancer-related genes that can be used to assess pathogenic single-nucleotide variants (SNV) and multiple-nucleotide variants, gene fusions, splice variants, copy number variants (CNVs), MSI, TMB, and ten oncogenic pathogens with both DNA and RNA simultaneously from FFPE samples. **Results:** From September 2017 to February 2022, a total of 91 patients were included in the study; 45 were assigned to NI and 46 to N-CT. With a median follow-up of 18 months, 1-year OS rate was 59.4% with NI and 56.7% with N-CT. Median OS and median PFS were 14.7 and 3.8 months in the NI arm and 12.9 and 6.3 months in the N-CT arm. Response rate was 24.4% with NI and 34.8% with N-CT. In the NI arm median OS was 13.9, not reached and 16.3 months in PD-L1 negative, PD-L1 low and PD-L1 high, respectively. In the N-CT arm median OS was 12.1, 13.8 and 11.7 months in PD-L1 negative, PD-L1 low and PD-L1 high, respectively. Biomarker analyses are ongoing and results are not available at the time of this analysis. **Conclusions:** Results of the SQUINT trial showed no difference between NI and N-CT for any clinical end-point. Correlative biomarker analyses will be presented at the meeting.

Patient Characteristics

	NI N= 45		N-CT N=46	
	N	100%	N	100%
Age, median (IQR)	69 (64-73)		69 (65-72)	
M/F	38/7	84/16	34/12	74/26
ECOG PS 0/1*	21/24	47/53	26/20	57/43
Never Smoker/Past Smoker/Current smoker	2/21/22	4/47/49	2/21/23	4/46/50
Stage IIIB/IV/recurrent	8/33/4	18/73/9	14/30/2	30/65/4
Number of disease sites, 1/2/>2	8/15/22	18/33/49	6/15/25	13/33/54
Brain metastases	2	4	4	9
Liver metastases	4	9	7	15
Bone metastases	10	22	14	30
PD-L1 TPS				
• <1%	10	22	12	26
• 1-49%	20	44	24	52
• ≥ 50%	8	18	10	22
• Unknown	7	16	0	0

*1 patient with PS 2 in ARM NI was included as PS 1

Registration numbers: EudraCT 2016-004003-31 - NCT03823625
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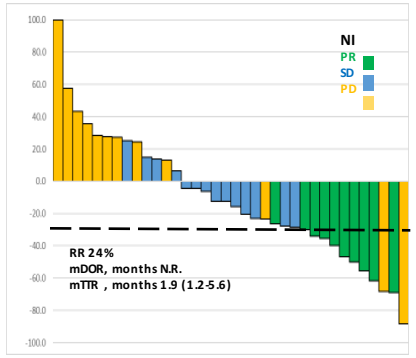
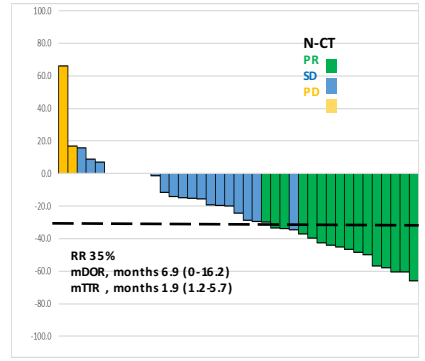
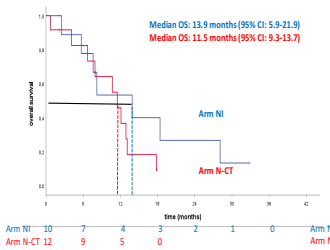
Best Percentage Change in Target Lesions



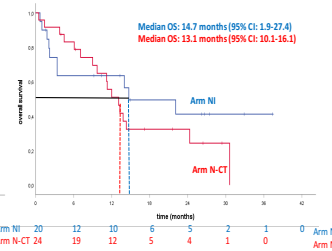


Overall Survival according to PD-L1 expression

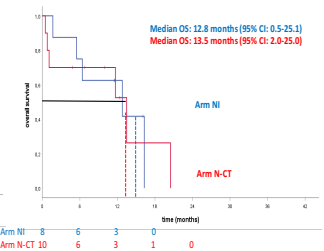
PD-L1 negative



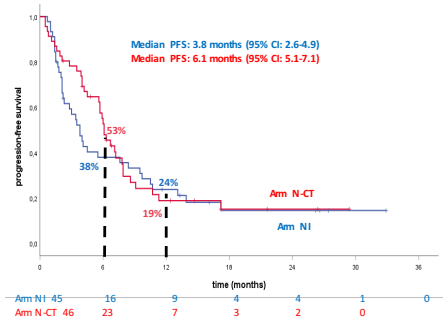
PD-L1 1%-49%



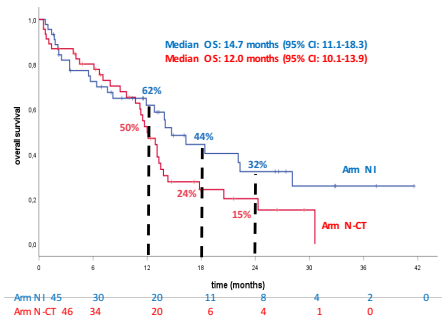
PD-L1 >=50%



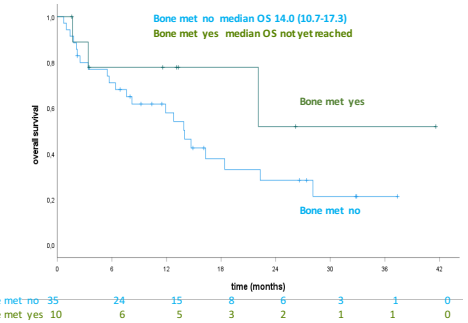
Progression Free Survival



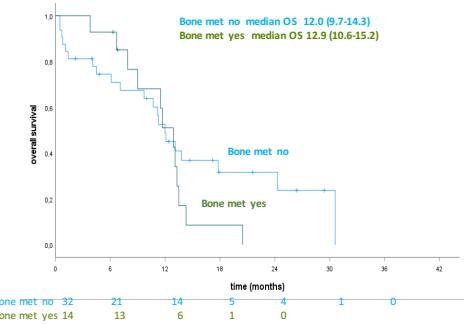
Overall Survival



OS according to bone mts - NI

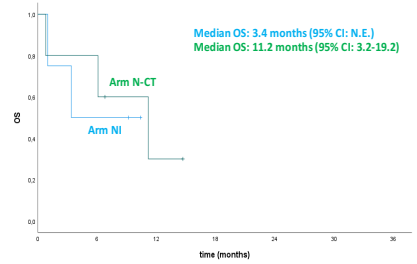


OS according to bone mts – N-CT

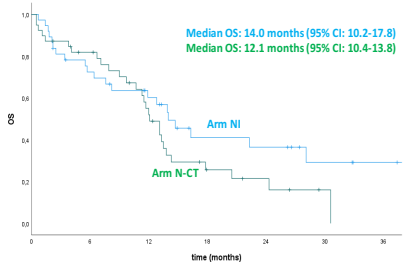


Overall Survival according to TMB

TMB low

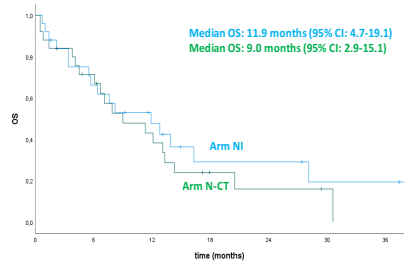


TMB high

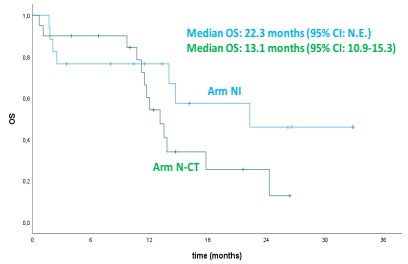


Overall Survival according to MSS/MSI status

MSS



MSI low



Median follow-up: 26 months

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