Final overall survival and safety update of a randomised, open-label, phase 3 study nivolumab plus ipilimumab versus carboplatin-based doublet as first-line treatment for patients with advanced non-small-cell lung cancer aged ≥70 years or with an ECOG performance status of 2 (ENERGY GFPC 08–2015)*

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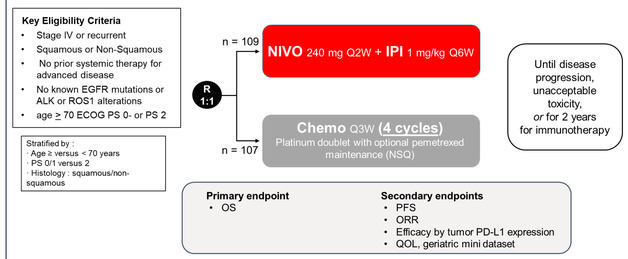
Background

- Elderly patients are underrepresented in phase III comparative IO studies while PS2 patients were excluded.
- CheckMate-227 showed durable response and OS benefit with nivolumab ipilimumab (NI) combination versus chemotherapy (chemo) in first line advanced NSCLC.
- ENERGY GFPC 08–2015 explore NI efficacy for elderly and/or PS2 NSCLC patients compared to carboplatin-based doublet

Methods

- Study design



- ENERGY GFPC 08–2015 was an open-label, multicentre, randomised, controlled, phase 3 trial open in 30 hospitals and cancer centres in France

- Statistical plan :

. ENERGY GFPC 08–2015 trial was calibrated to detect an improvement of 1-year OS rate from 40% (chemo arm) to 55% (NI arm), equivalent to HR of 0.65 (with a power of 85% and alpha level of 5%)

. pre-planned interim analysis after randomisation of 217 patients (242 planned) and 33% of the expected events.

. efficacy analyses were performed in the intention-to-treat population,

. Safety analysis were performed in the safety analysis set (all randomly assigned patients who received at least one dose of study treatment and who had at least one safety follow-up)

Results

- Baseline characteristics

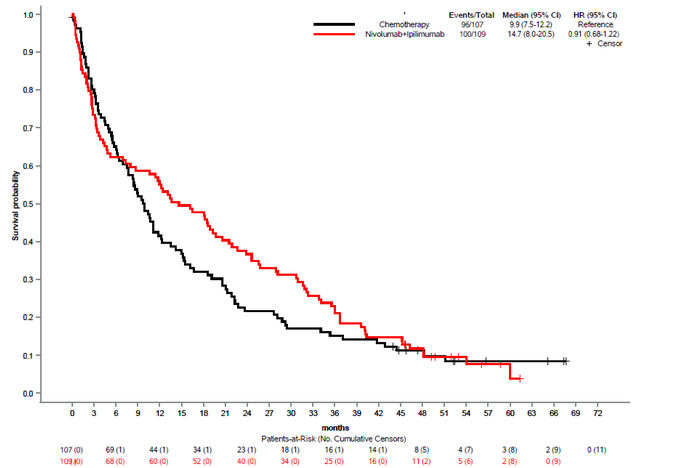
	NIVO + IPI (n = 109)	Chemo (n = 107)
Age, median (range), years	74 (52-89)	74 (51-88)
≥ 70	78%	79.4%
Female, %	32.1	25.2
ECOG PS, %		
0	26.6	25.2
1	37.6	37.4
2	35.8	37.4
Smoking status, %		
Never smoker	11.9	8.4
Current / former smoker	88.1	91.6
Histology, %		
Squamous	32.1	30.8
Non-squamous	67.9	69.2
Metastases, %		
Bone	37.6	43.9
Liver	14.7	16.8
CNS	8.3	7.5
Tumor PD-L1 expression,%		
<1%	58.7	54.1
1–49%	38.5	37.8
≥ 50%	2.9	8.2
ND	4.5	8.4

- Safety analysis

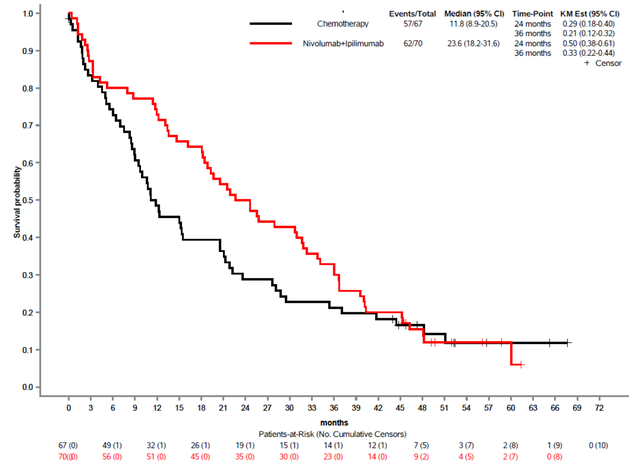
	Nivolumab plus ipilimumab (N=105)		Chemotherapy (N=103)	
	All grades	Grade ≥ 3	All grades	Grade ≥ 3
Blood and lymphatic system disorders	25 (23·8)	1 (1·0)	69 (67·0)	41 (39·8)
Anaemia	14 (13·3)	0	49 (47·6)	9 (8·7)
Neutropenia	2 (1·9)	0	42 (40·8)	28 (27·2)
Thrombocytopenia	5 (4·8)	0	20 (19·4)	5 (4·9)
Cardiac disorders	14 (13·3)	10 (9·5)	9 (8·7)	6 (5·8)
Endocrine disorders	15 (14·3)	5 (4·8)	0	0
Gastrointestinal disorders	56 (53·3)	11 (10·5)	51 (49·5)	4 (3·9)
Constipation	21(20·0)	2 (1·9)	11 (10·7)	0
Diarrhoea	27 (25·7)	3 (2·9)	25 (24·3)	2 (1·9)
Nausea	13 (12·4)	0	28 (27·2)	2 (1·9)
Vomiting	8 (7·6)	0	15 (14·6)	0
General disorders and administration site conditions	73 (69·5)	17 1(6·2)	70 (68·0)	16 (15·5)
Asthenia	59 (56·2)	9 (8·6)	56 54·4)	9 (8·7)
Chest pain	11 (10·5)	3 (2·9)	5 (4·9)	1 (1)
Hepatobiliary disorders	11 (10·5)	7 (6·7)	3 (2·9)	2 (1·9)
Infections and infestations	46 (43·8)	19 (18·1)	32 (31·1)	14 (13·6)
Pneumonia	14 (13·3)	7 (6·7)	8 (7·8)	5 (4·9)
Metabolism and nutrition disorders	34 (32·4)	11 (10·5)	29 (28·2)	7 (6·8)
Decreased appetite	14 (13·3)	2 (1·9)	18 (17·5)	2 (1·9)
Musculoskeletal and connective tissue disorders	36 (34·3)	4 (3·8)	17 (16·5)	0
Arthralgia	15 (14·3)	1 (1·0)	3 (2·9)	0
Back pain	15 (14·3)	3 (2·9)	3 (2·9)	0
Nervous system disorders	32 (30·5)	8 (7·6)	28 (27·2)	4 (3·9)
Neuropathy peripheral	10 (9·5)	0	18 (17·5)	1 (1)
Psychiatric disorders	16 (15·2)	4 (3·8)	9 (8·7)	3 (2·9)
Renal and urinary disorders	16 (15·2)	8 (7·6)	5 (4·9)	1 (1)
Acute kidney injury	11 (10·5)	6 (5·7)	2 (1·9)	0
Respiratory, thoracic and mediastinal disorders	44 (41·9)	20 (19·0)	36 (35·0)	12 (11·7)
Dyspnoea	14 (13·3)	1 (1·0)	16 (15·5)	3 (2·9)
Skin and subcutaneous tissue disorders	43 (41·0)	4 (3·8)	21 (20·4)	1 (1·0)
Alopecia	1 (1·0)	0	11 (10·7)	0
Pruritus	23 (21·9)	0	2 (1·9)	0
Vascular disorders	18 (17·1)	4 (3·8)	14 (13·6)	6 (5·8)

- Efficacy Analysis

- **Overall survival (entire population)**



- **Overall survival (PS 0-1)**



CONCLUSIONS

- With longer follow up, the trial is still negative regarding the entire population.
- NI shows clinical signal of efficacy in patients aged ≥70 with advanced NSCLC and PS 0–1, with QoL maintained over time
- Dedicated trials for geriatric and poor PS NSCLC patients must be developed in order to provide best options regarding efficacy and toxicity

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