Real-life efficacy of nivolumab plus ipilimumab combination in untreated, unresectable malignant pleural mesotheliomas: Result of French early access program. MESOIMMUNE – GFPC 04-2021

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Authors: O. Bylicki[1], F. Guisier[2], C. Daniel[3], A. Swalduz[4], E. Grolleau[5], M. Bernardi[6], S. Hominal[7], N. Cloarec[8], S. Deshayes[9], J. Raimbourg[10], R. Veillon[11], Y. Oulkhouir[12], C. Audigier Valette[13], A. Gobert [14], L. Falchero[15], L. Thibonnier [16], M. Chasseray[17], C. Raynaud[18] and C. Decroisette[4] ,L. Greillier[19], on behalf of GFPC.

1. Hôpital d'Instruction des Armées Sainte Anne, Toulon; 2. CHU Rouen, Rouen; 3. Institut Curie Hospital, Paris; 4. Léon Bérard Cancer Center, Lyon; 5. Louis-Pradel Hospital, Hospices Civils de Lyon; 6. Aix-en-Provence Hospital, Aix-en-Provence; 7. Centre Hospitalier Annecy-Genevois, Pringy; 8. CH Henri Duffaut, Avignon; 9. CHU Caen, Caen; 10. Institut de Cancérologie de l'Ouest, Nantes; 11. CHU Bordeaux, Bordeaux; 12. CHU ANGERS, Angers; 13. Centre hospitalier Toulon Sainte-Musse, Toulon; 14. Clinique St Grégoire, Rennes; 15. L'Hôpital Nord-Ouest, Villefranche Sur Saône; 16. Clermont-Ferrand University Hospital, Clermont-Ferrand; 17. Clinique Pasteur, Brest; 18. Centre hospitalier d'Argenteuil, Argenteuil; 19. Hôpital Nord, Assistance Publique-Hôpitaux de Marseille, Marseille.

GFPC
Groupe Français de Pneumo-Cancérologie
French Lung Cancer Group

Background

- The standard of care for unresectable malignant pleural mesothelioma (MPM) has changed in 2020 with the results of CheckMate 743 study (1,2).
- This phase III study aimed to assess efficacy and safety of first line nivolumab plus ipilimumab (NIVO+IPI) versus platinum plus pemetrexed chemotherapy in unresectable MPM. NIVO+IPI significantly extended overall survival (OS) versus chemotherapy (median OS 18.1 months vs 14.1 months, HR 0.74, p=0.0020).
- As CheckMate 743 was therapeutic trial in selected MPM patients, additional data would be of interest to confirm the results in real-life setting.

Study Design:

- The MESO-IMMUNE study (GFPC 04–2021) was a national retrospective non-interventional study that included patients treated with nivolumab and ipilimumab in the French early access program.
- Inclusion criteria :
  - At least 18 years old;
  - Untreated and unresectable Malignant Pleural Mesothelioma;
  - Treatment with nivolumab 360 mg every three week and Ipilimumab 1mg/kg every six weeks in the setting of the early access program from April 1, 2021, to Feb 15, 2022.

Objective:

- The primary objective was **investigator-assessed real world progression-free survival** (rwPFS) from initiation of NIVO+IPI, defined as time from first dose of NIVO+IPI to first documentation of objective disease progression or death from any cause.
- The secondary objectives were real world OS (rwOS), objective response rate (ORR), and safety of NIVO+IPI combination.

(1) Baas P, Scherpereel A, Nowak AK, et al. Lancet. 2021 Jan 30;397(10272):375-386.
(2) Peters S, Scherpereel A, Cornelissen R, et al. Ann Oncol. 2022 May;33(5):488-499

Clinicopathological characteristics

- From April 1, 2021 to Feb 15, 2022 (last day of EAP) there were 143 patients included out of 350 patients treated by EAP for unresectable MPM in 44 centers. Population characteristics are described in Table 1.

Table 1 Baseline characteristics

	Nivolumab + Ipilimumab (n=143)
Age, years (SD)	74.8 (9.42)
<65	20 (14.0%)
≥ 65 to ≤ 75	45 (31.5%)
≥ 75	78 (54.5%)
Sex	
Male	120 (83.9%)
Female	23 (16.1%)
Eastern Cooperative Oncology Group Performance status	
0	51 (39.8%)
1	66 (51.6%)
2	9 (7.0%)
≥2	2 (1.6%)
Smoking Status	
Current or former	71 (49.7%)
Never	64 (44.8%)
Unknown	13 (05.6%)
Comorbidities	
Hypertension	88 (55.9%)
Heart disease	43 (30.1%)
Others Cancers	29 (20.3%)
COPD	5 (3.5%)
asbestos exposure	
Yes	88 (61.5%)
of professional origin	85 (59.4%)
No	39 (27.3%)
Unknown	16 (11.2%)
Histology	n=142
Epithelioid	99 (69.7%)
Non-Epithelioid	43 (30.3%)
Sarcomatoid	13 (9.2%)
Mixed or other	30 (21.2%)
Stage	n=98
1	9 (9.2%)
2	10 (10.2%)
3	49 (50.0%)
4	30 (30.6%)

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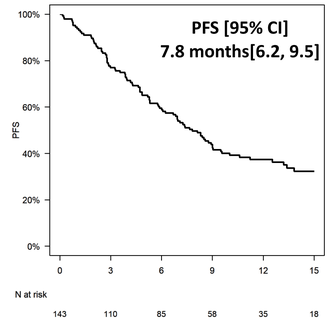
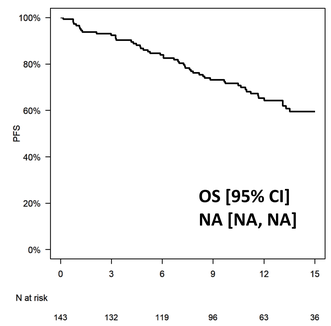
Efficacy

- With a median follow-up of 14.1 months
- **Figure 1. real-world PFS for entire population**



- **1-year survival rate was 65% (95% CI 57-75%)**
- **Figure 2. real-world OS for entire population**



- **Table 2 Efficacy by histological subtype**

	Epithelioid MPM N=99	Non-epithelioid MPM N=43
Objective response rate (ORR)	20.4%	30.0%
95% CI	(12.8-30.1%)	(16.6-46.5%)
rw-PFS (mo.) 95% CI	8.1(6.0-12.6)	7.4 (5.3-11.2)
rw-OS (mo.) 95% CI	NA (NA-NA)	13.1 (7.8-NA)
1-year OS 95% CI	71%(62.5-81.1%)	51.2%(37.7-69.4%)

TOLERANCE

	Population n=143	
	Any grade	Grade 3-4
Adverse event of any cause		
All	85 (60.7%)	31 (37.8%)
Leading to study drug discontinuation	31 (36.9%)	
Leading to study drug interruption	13 (15.5%)	
Serious	34 (40.5%)	
Death	5 (3.5%)	
Asthenia	2	
Hepatocellular damage	1	
Renal failure	1	
Respiratory failure	1	
Adverse event of any grade in ≥10 of patients		
Asthenia	31 (21.7%)	4 (2.8%)
Gastrointestinal disorders	27 (18.9%)	3 (2.1%)
Musculoskeletal and connective tissue pain and discomfort	23 (16.1%)	4 (2.8%)
Rashes, eruptions and exanthems	25 (17.5%)	0
Breathing abnormalities	18 (12.6%)	9 (6.3%)
Endocrine disorders	13 (9.1%)	1 (0.7%)
Hypothyroidism	6 (4.2%)	0
Hyperthyroidism	4 (2.8%)	0
Hypophysitis	3 (2.1%)	0
Diabetes	1 (0.7%)	1 (0.7%)

CONCLUSIONS

- ✓While patient's characteristics differed from the pivotal trial, notably with older and unselected patients, efficacy outcomes that we observed here compares favorably with CheckMate 743 results.
- ✓Tolerance looks acceptable in real-life setting despite 5 toxic deaths reported.
- ✓Extended follow-up of our cohort will allow consolidation of the results.

Fundings

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