PD-L1 Expression as a Prognostic Factor of Overall Survival in Patients with Malignant Pleural Mesothelioma.

PO-087

"National medical research center of Oncology named after N. N. Blokhin". The Moscow state medical University named after A. I. Evdokimov.

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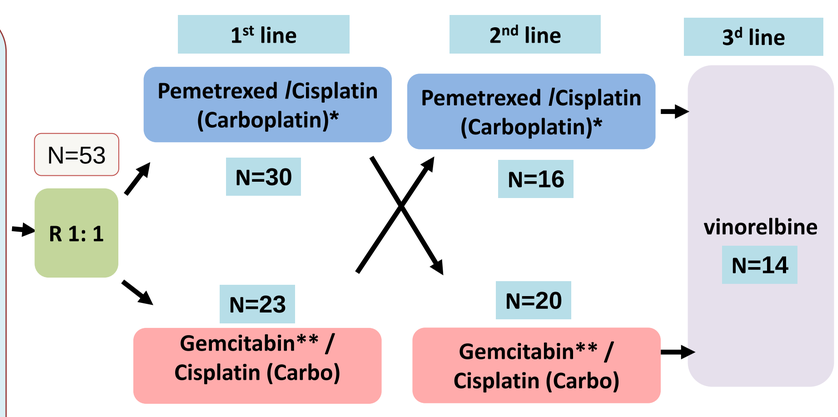
Study design

- Unresectable malignant pleural mesothelioma
- All histological types
- IHC confirmation
- Target lessons (mRECIST 1.1)
- ECOG 0–2
- No prior chemotherapy
- Age ≥18
- Life expectancy ≥ 3 months
- No brain mts



*500 mg/m² / 75 mg/m² / AUC-5 IV, w3. Max 6 cycles.
** 1200 mg/m² IV 1, 8 days, w3. Max 6 cycles.
Duration of treatment – 18 weeks Duration of observation - 28 month

Table 1. Patients characteristics

		PemPt 1st L. (n30)	GemPt 1st L. (n23)	PemPt 2nd L. (n16)	GemPt 2nd L. (n20)	Vin 3rd L. (n14)
Age, mediana		58.6	53.4	54.1	57.9	57.8
Age; n (%)	< 65	20 (67)	14 (61)	15 (94)	17 (85)	9 (64)
	≥ 65	10 (33)	9 (39)	1 (6)	3 (15)	5 (36)
Sex; n (%)	Male	16 (53)	12 (52)	7 (44)	12 (60)	9 (64)
	female	14 (47)	11 (48)	9 (56)	8 (40)	5 (36)
ECOG; n (%)	0	9(30)	8 (35)	2 (13)	1 (5)	0
	1	19 (63)	11 (48)	10 (63)	10 (50)	4 (29)
	2	2 (7)	4 (17)	4 (25)	9 (45)	10 (71)
Stage; n (%)	II	4 (13)	3 (13)	4 (25)	4 (20)	2 (21)
	III	8 (27)	6 (26)	8 (50)	7 (35)	2 (14)
	IV	18 (60)	14 (61)	12 (75)	9 (45)	9 (65)
Histology; n (%)	Epith.	26 (87)	19 (83)	15 (94)	16 (80)	12 (86)
	Non-epith.	4 (13)	4 (17)	1 (6)	4 (20)	2 (14)
PD-L1 (30 tumor blocks)	(-)	7 (23)	5 (42)	-	-	-
	(+)	11 (37)	7 (58)	-	-	-

Purpose

To evaluate the role of PD-L1 expression as a prognostic factor of OS in patient with malignant pleural mesothelioma (MPM)

Material and methods

From Jan 2006 to Nov 2016, 53 pts with II-IV stage MPM were underwent 1-line treatment with pemetrexed or gemcitabine with cisplatin or carboplatin. After the progression there was a crossover of groups. Vinorelbine was prescribed in the 3d line. Tumor tissue samples were obtained by thoracoscopic biopsy of the primary tumor. Pts didn't receive any therapy prior to receiving tumor samples. IHC was performed on sections filled in paraffin on an automatic immunohistostainer of the Ventana BenchMark series in combination with diagnostic kits. Tonsil tissue was used as a positive control for PD-L1. As control tissues, fresh autopsy, biopsy or surgical samples were used, prepared and fixed by a method similar to that for the studied sections. When evaluating PD-L1 expression using the anti-PD-L1 antibody [platform 28.8] ab205921, only the membrane staining of tumor cells was taken into account, regardless of the intensity and completeness of cell membrane staining (partial, subtotal, complete). The color of the nuclei and cytoplasm of tumor cells, the color of antigen-presenting and lymphoid cells in the tumor were not taken into account. Samples with a PD-L1 expression less than 5% were regarded as negative, 6% or more as positive. 18/30 tumor blocks (60%) were positive for PD-L1 expression. Additionally, an analysis was carried out depending on the proportion of stained cells. Stratification factor was PD-L1 score. Primary endpoints were ORR, safety. Secondary: OS, PFS.

Table 2. Distribution of patients depending on the proportion of PD-L1-positive tumor cells.

Proportion of PD-L1-positive tumor cells	n	%
≤ 5%	12	40
>5% < 50%	8	26.7
≥50%	10	33.3

The relationship between PD-L1 expression and the histological subtype of MPM was noted. Epithelioid type was found in 22 (73.3%) pts. At the same time, there were 55% with a negative PD-L1 (12/22), 36% with an average expression level (8/22), and 9% with a high expression level (2/22)

Table 3. Distribution of patients depending on the histological type of tumor and PD-L1 expression.

Proportion of PD-L1-positive tumor cells	Epithelioid (n-22)	Non-epithelioid (n-8)
≤ 5%	12 (55%)	-
>5%< 50%	8 (36%)	-
≥50%	2 (9%)	8 (100%)

Results

	PemPt	GemPt
mPFS(95% CI); month	12,6 (3-34)	10,6 (3–43)

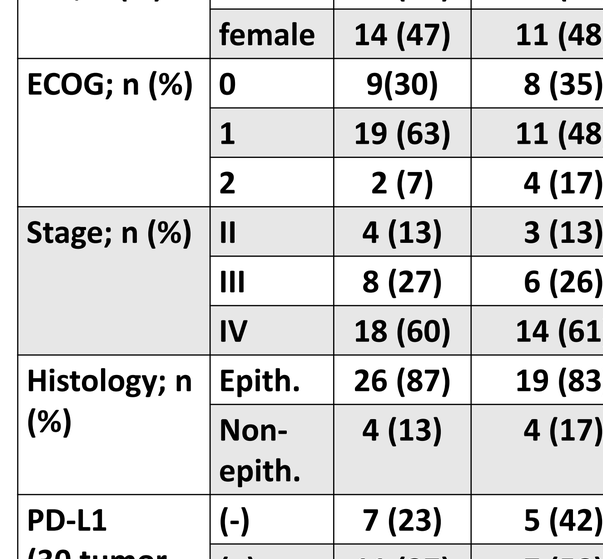


Figure 1. PFS, 1st L PemPt vs GemPt in MPM

	PemPt	GemPt
mOS (95% CI)	22,4 (7,3-122)	23,5 (3,3–61,5)

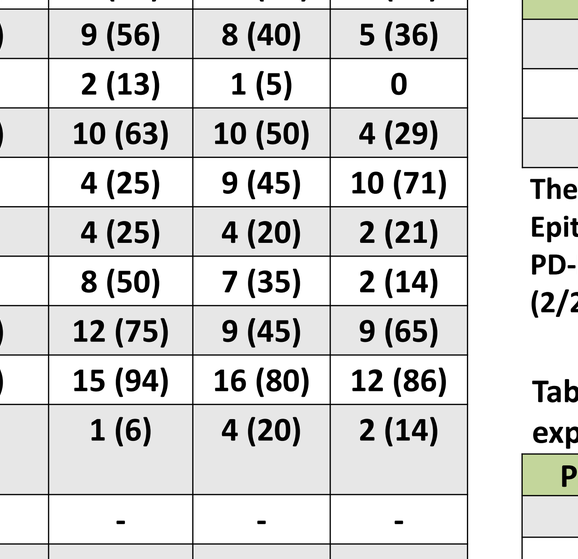


Figure 2. OS, 1st L PemPt vs GemPt in MPM

	PemPt	GemPt
mPFS (95% CI); month.	8,0 (1,5-45)	5,4 (3–43)

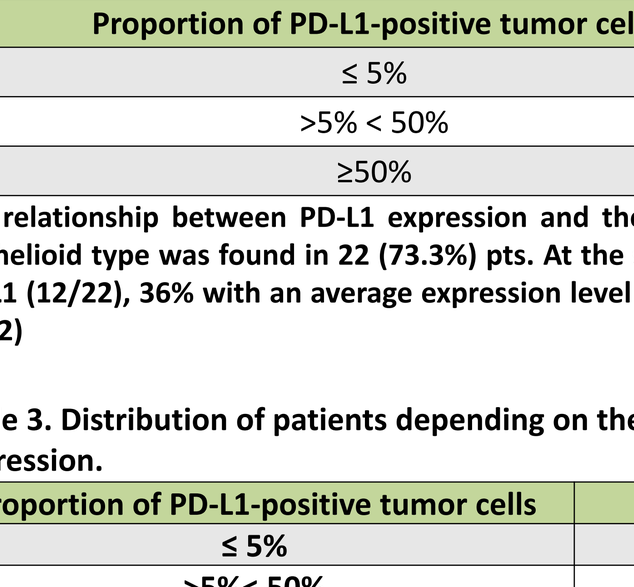


Figure 3. PFS, 2nd L PemPt vs GemPt in MPM

	PemPt	GemPt
mOS (95% CI); month	18,5 (2,8-47)	15,5 (2,3–86)

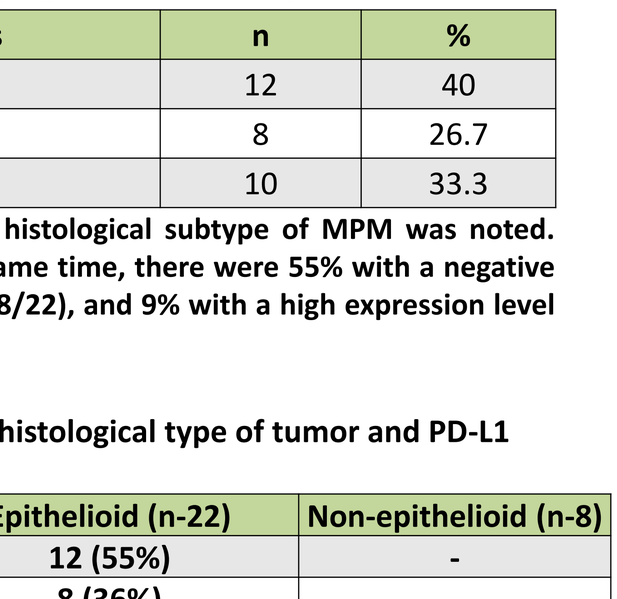


Figure 4. OS, 2nd L PemPt vs GemPt in MPM

mPFS (95% CI); month.	3,0 (1,5-12,8)

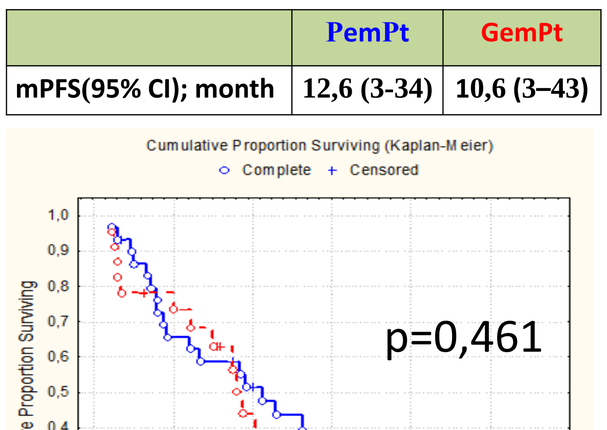


Figure 5. PFS, 3d L vinorelbine in MPM

mOS (95% CI); month.	5,2 (1,5-58)

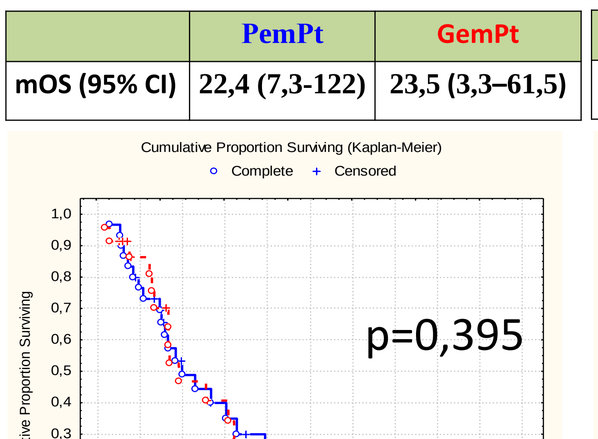


Figure 6. OS, 3d L vinorelbine in MPM

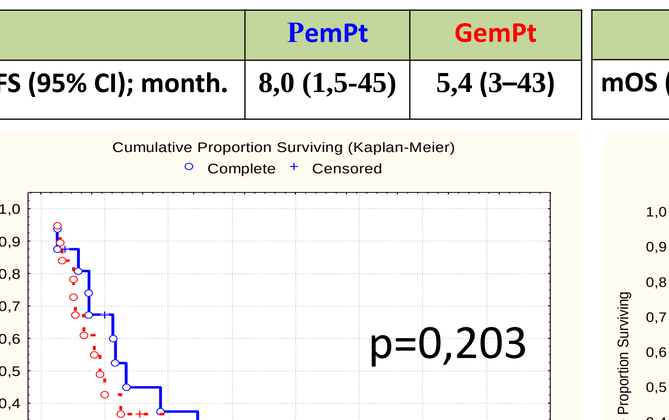


Figure 7. Overall survival curve depending on PDL-1 expression in tumor cells in MPM

In our study, PD-L1 expression in the tumor cells correlates with long-term results. PD-L1-negative pts demonstrates higher OS vs to the group where PD-L1 is positive.
mOS with PD-L1 positive status is 15.6 months, while with negative status 41.0 months
(p=0.00294 Cox's f-test. p=0.00188 Long-Rank test)

Conclusion

The effectiveness of pemetrexed/platinum and gemcitabine/platinum in the 1st line of treatment for MPM is comparable. The OR was achieved in 30% with Pem and in 35% with Gem. The mPFS was 12.6 and 10.6 months, respectively. The mOS was 22.4 and 23.5 months. The effectiveness of 2nd line chemotherapy with the same combined regimens is comparable between groups. An OR was noted in 18.8% in the pemetrexed group and 5% in the gemcitabine group (p<0.2). The mPFS was 8 and 5.4 months. The mOS was 18.5 and 15.5 months, respectively. Vinorelbine in the 3d line of chemotherapy for MMP is ineffective. The OR was achieved in 7.1% of pts, mPFS - 3 months, mOS - 5.2 months, 2-year survival - 7.1%.

Our data show that MPM expresses PD-L1 in 60% of cases, which is associated with a poor prognosis. In the non-epithelioid type, PD-L1 expression is more common than in the epithelioid type. The 2- and 3-year OS of pts with negative PD-L1 tumor were 100 and 73%, respectively, whereas for positive PD-L1 these indicators were 26 and 19.1%. PD-L1 expression is a prognostic marker of life expectancy in pts with MPM.