FPN: 300P

Correlation of PD-L1 protein and mRNA expression and their prognostic impact in triple negative breast cancer

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Background and Methods

Background and Aims

- PD-L1 expression is determined by immunohistochemical (IHC) analyses.
- PD-L1 positivity can differ depending on the used antibody.
- Aim: Correlation of PD-L1 IHC and mRNA expression and association with prognosis

Material and Methods

- Patients: PiA Prognostic Assessment in routine application (NCT 01592825)
- PD-L1 IHC was performed using CAL10 antibody (BioCare).
- Positivity defined as ≥1% staining for immune cell score (IC), tumour proportion score (TPS), combined positive score (CPS)
- PD-L1 mRNA expression determined by microarray analysis (Affymetrix®, HG U133 Plus 2.0, probesets #1: 223824, #2: 227458)
- Maximum likelihood method used for cut off determination
- Correlations with PD-L1 IHC and TILs tested using Spearman´s rank correlation
- Survival: recurrence free interval (RFI) and overall survival (OS)
- Median follow up was 73 months (20-127).

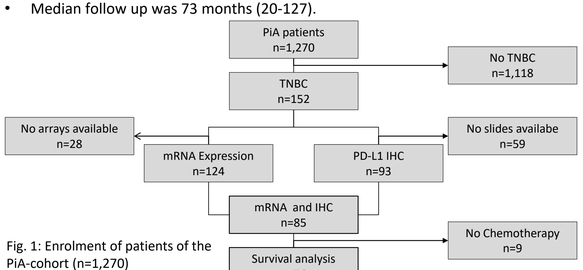

Fig. 1: Enrolment of patients of the PiA-cohort (n=1,270) for PD-L1 analysis

Results

Tab. 1: Patient and tumour characteristics

	TNBC entire cohort (n=152) n (%)	mRNA analysis (n=124) n (%)	IHC analysis (n=93) n (%)
Age at diagnosis			
< 50	56 (36.8)	43 (34.7)	28 (30.2)
51-75	74 (48.7)	60 (48.4)	46 (49.5)
> 75	22 (14.5)	21 (16.9)	19 (20.4)
Tumour histology			
ductal (NST)	131 (86.2)	106 (85.5)	82 (88.2)
lobular	7 (4.6)	4 (3.2)	2 (2.2)
others	14 (9.2)	14 (11.3)	9 (9.7)
Tumour size at time of diagnosis			
< 2cm	46 (30.3)	41 (33.1)	36 (38.7)
2-5cm	84 (55.3)	68 (54.8)	51 (54.8)
> 5cm	22 (14.5)	15 (12.1)	6 (6.5)
Nodal status at time of diagnosis			
negative	77 (50.7)	64 (51.6)	51 (54.8)
positive	75 (49.3)	60 (48.4)	42 (45.2)
Tumour differentiation			
G1	1 (0.7)	1 (0.8)	1 (1.1)
G2	60 (39.5)	50 (40.3)	39 (41.9)
G3	91 (59.9)	73 (58.9)	53 (57.0)

- In IHC analysis, half of the samples were classified PD-L1 positive for IC and CPS (50.6% and 49.4%) and only 23.5% considering TPS

Tab. 2: Distribution of PD-L1 IHC, n=93

	IC	TPS	CPS
Positive	50.6 %	23.5%	49.4%
Negative	49.4 %	76.5%	50.6%
Mean	2.2%	5.3%	6.4%

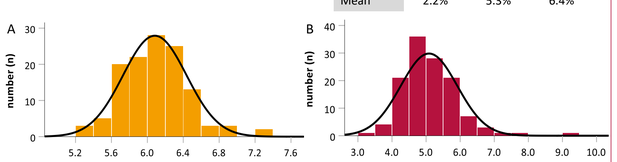

Fig. 2: Distribution of PD-L1 mRNA expression, A) Probeset #1 B) Probeset #2; n=124

- In probeset #1, 63.5% were determined PD-L1 positive
- In probeset #2 only 34.1% showed a PD-L1 positivity

Results

- In probeset #1, no correlation to the IHC scores, TILs and probeset #2 was shown.
- Probeset #2 had a strong correlation with the IHC scores and to TILs (p<0.01).

Tab. 3: Spearman correlation of the following factors; * p<0.01

	TILs	Probeset #1	Probeset #2	IC	TPS	CPS
TILs	1					
Probeset #1	0.027	1				
Probeset #2	0.489*	**-0.015**	1			
IC	0.571*	0.039	0.570*	1		
TPS	0.329*	0.047	0.469*	0.647*	1	
CPS	0.538*	-0.010	0.592*	0.943*	0.769*	1

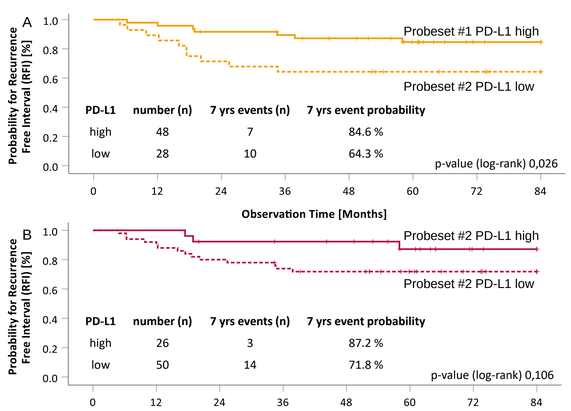

Fig. 3: Kaplan–Meier plots for patients in PD-L1 PD_L1.1 (A) and PD-L1.2 (B) Presented with number, events and 7 years event probability

Results and Conclusion

- PD-L1 had no impact on survival when determined by IHC or probeset #2.
- In contrast, patients with high PD-L1 expression in probeset #1 had a more favourable 7-years RFI probability (84.6% vs 64.3%).
- Low PD-L1 expression in probeset #1 showed higher risk for recurrence in univariate (2.68, 95%CI 1.089-7.532) and multivariate analysis (3.43, 95%CI 1.294-9.080, adjusted to nodal status)
- Considering OS only a trend was shown (HR 1.45, 95%CI 0.570-3.662).

Tab. 4: Cox proportional Hazard Ratio od PD-L1 mRNA expression, considering RFI and OS, univariate analysis (n=76)

	RFI			OS		
	HR	95%CI	*p-value*	HR	95%CI	*p-value*
Probeset #1	**2.86**	**1.089-7.532**	***0.033***	1.45	0.570-3.662	*0.438*
Probeset #2	2.69	0.772-9.351	*0.120*	2.88	0.831-9.918	*0.096*

Tab. 4: Cox proportional Hazard Ratio od PD-L1 mRNA expression, considering RFI and OS multivariate analysis, adjusted to nodal status (n=76)

	RFI			OS		
	HR	95%CI	*p-value*	HR	95%CI	*p-value*
Probeset #1	**3.43**	**1.294-9.080**	***0.013***	1.81	0.707-4.605	*0.217*
Probeset #2	2.71	0.778-9.437	*0.117*	3.01	0.870-10.434	*0.082*

Conclusion:

- In the evaluable patients of our cohort, the PD-L1 mRNA analysis detected additional PD-L1 positive tumours compared to IHC analysis.
- For validation of the prognostic impact and to examine the predictive value considering therapy with immune checkpoint inhibitors, further studies are warranted.
- Variable mRNA expression may be one reason why immune checkpoint inhibitors show benefit for patients independent from PD-L1 IHC status.

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Contact

This presentation is the intellectual property of the authors. The presenting author has nothing to declare.

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