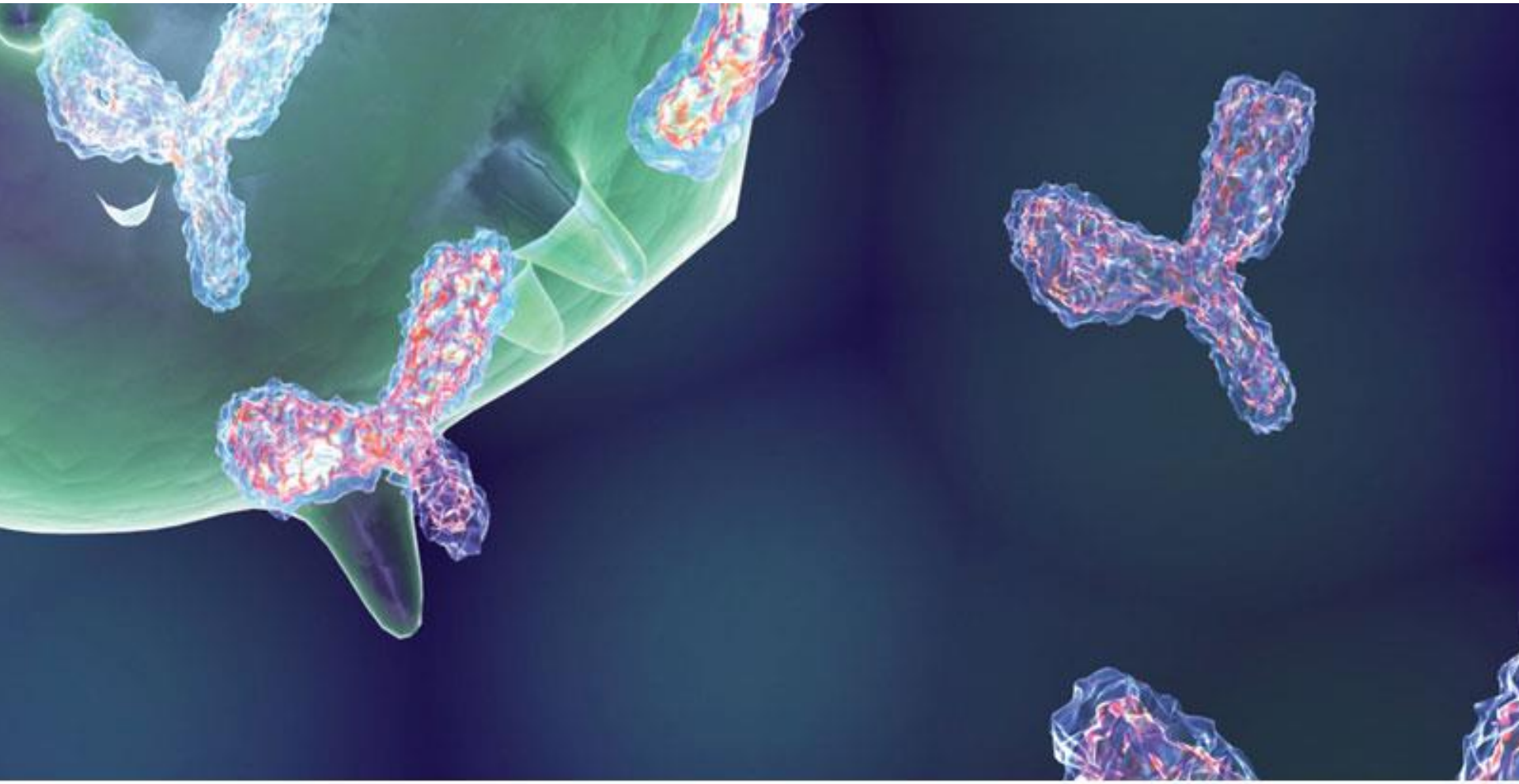
NHS
Greater Glasgow and Clyde

PDL1

Introducing a Companion Diagnostic

Dr Craig Dick

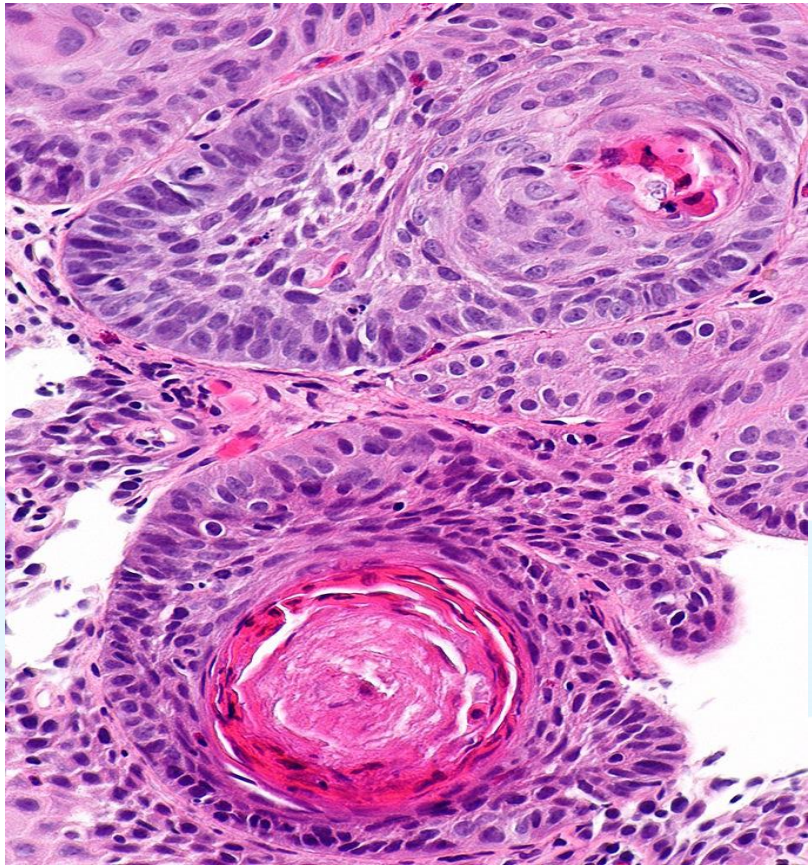
PDL1- Why, What and How?

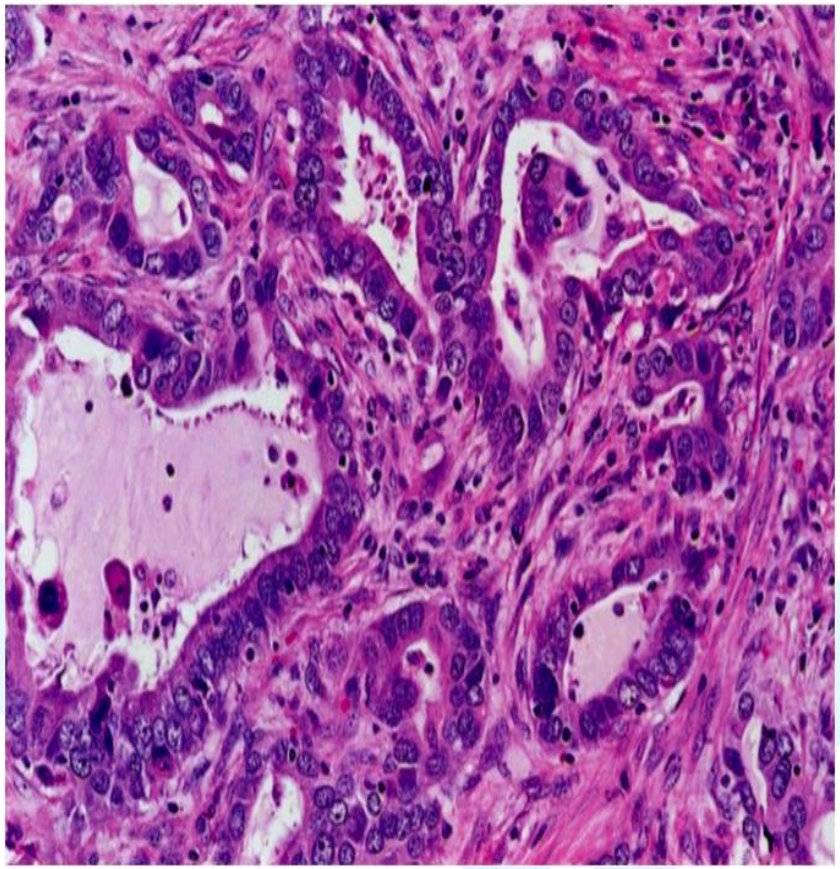


Why?

- There is a disease (Lung cancer).
- There is a treatment (Pembrolizumab).
- There is a test that predicts a response to the treatment.(PDL-1 on tumour cells)
- There are trials that has shown this works. (Keynote Trials)

Lung Cancer

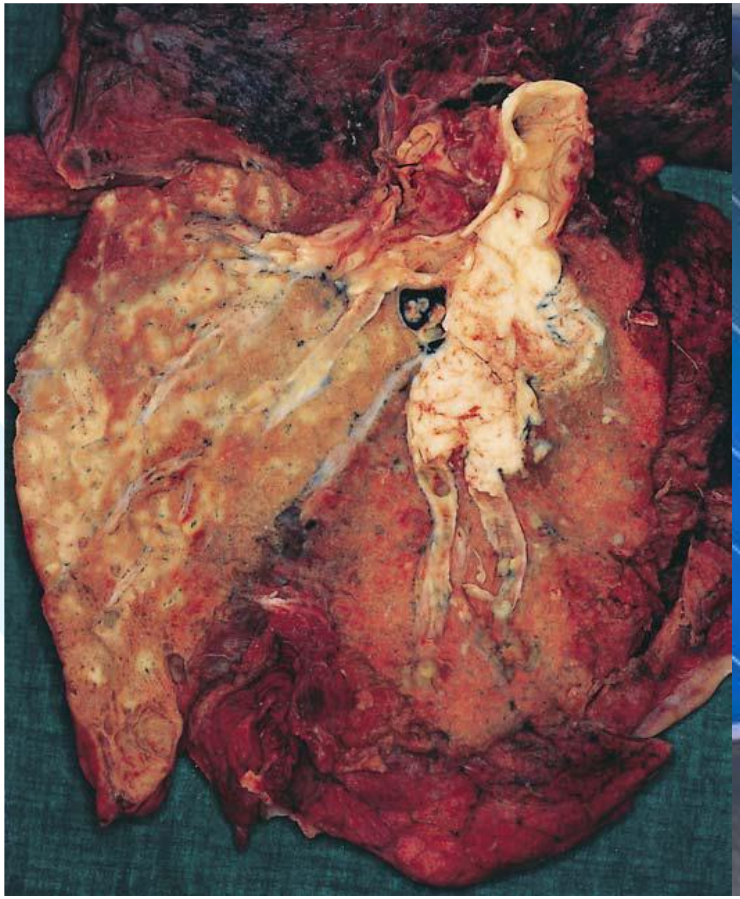




Lung Cancer

Age group	Period of diagnosis	Number of cases analysed	Observed survival (%) at 1 yr	3 yr	5 yr	10 yr	Relative survival (%) at 1 yr	3 yr	5 yr	10 yr
15-74	1987-1991	14,462	25.5	10.1	7.6	5.2	26.0	10.8	8.4	6.6
	1992-1996	14,320	27.7	10.9	8.2	5.6	28.2	11.5	9.1	7.0
	1997-2001	13,192	30.9	12.0	9.0	6.2	31.5	12.6	9.8	7.5
	2002-2006	12,602	33.0	13.1	9.5	5.9	33.5	13.7	10.4	7.2
	2007-2011	12,698	36.9	16.4	12.4	..	37.4	17.1	13.4	..
15-99	1987-1991	19,990	21.2	7.9	5.8	3.8	22.0	8.7	6.7	5.2
	1992-1996	20,445	23.4	8.7	6.3	4.1	24.2	9.6	7.4	5.6
	1997-2001	20,050	26.4	9.6	6.9	4.6	27.3	10.5	8.0	6.0
	2002-2006	20,234	28.4	10.5	7.4	4.4	29.3	11.4	8.4	5.8
	2007-2011	21,217	32.0	13.4	9.6	..	33.0	14.4	10.8	..

Lung Cancer Treatment



Lung Cancer
KEYNOTE TRIALS

- KEYTRUDA/Pembrolizamab
- KEYNOTE 10
- KEYNOTE 24

KEYNOTE 10

Patients
- Advanced NSCLC
- Confirmed disease progression after ≥1 line of chemotherapy[a]
- No active brain metastases
- ECOG PS 0–1
- PD-L1 TPS ≥1%
- No serious autoimmune disease
- No ILD or pneumonitis requiring systemic steroids

Stratification factors:
- ECOG PS (0 *vs.* 1)
- Region (East Asia *vs.* non-East Asia)
- PD-L1 status[b] (TPS ≥50% *vs.* 1%–49%)

R
1:1:1

Pembrolizumab 2 mg/kg IV Q3W, for 24 months until disease progression or unacceptable toxicity

Pembrolizumab 10 mg/kg IV Q3W for 24 months until disease progression or unacceptable toxicity

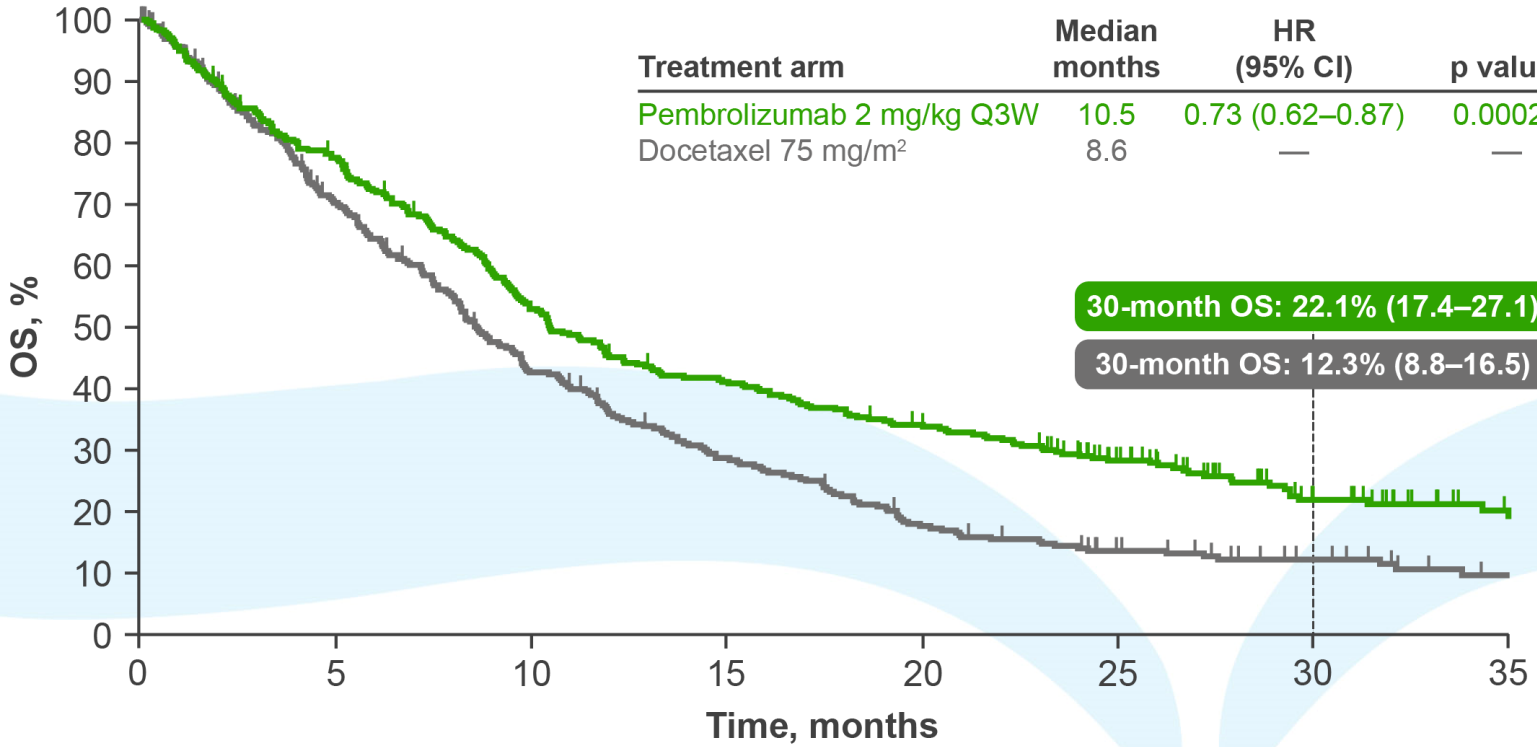
Docetaxel 75 mg/m^2 Q3W per local guidelines[c]

Endpoints stratified by TPS ≥50% *vs.* ≥1%
- Primary: PFS and OS
- Secondary: ORR, duration of response, safety

Adapted from: Herbst RS et al. Lancet 2016.

KEYNOTE-010: Pembrolizumab *vs.* docetaxel for **previously treated**, PD-L1-positive, advanced non-small-cell lung cancer

PD-L1 Tumour Proportion Score (TPS) ≥1%



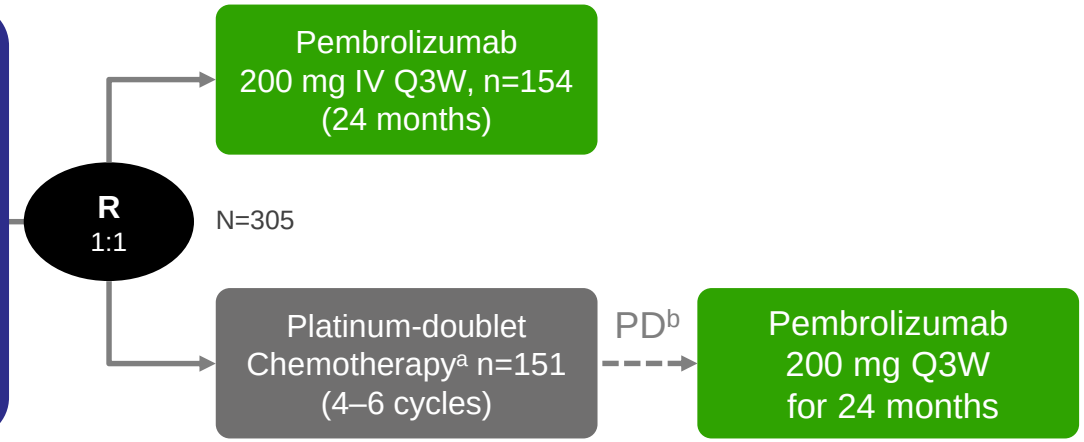
Treatment arm	Median months	HR (95% CI)	p value[b]
Pembrolizumab 2 mg/kg Q3W	10.5	0.73 (0.62–0.87)	0.00024
Docetaxel 75 mg/m²	8.6	—	—

No. at risk								
Pembrolizumab 2 mg/kg Q3W	344	261	176	135	110	75	36	16
Docetaxel 75 mg/m²	343	216	129	84	50	32	19	9

KEYNOTE 24

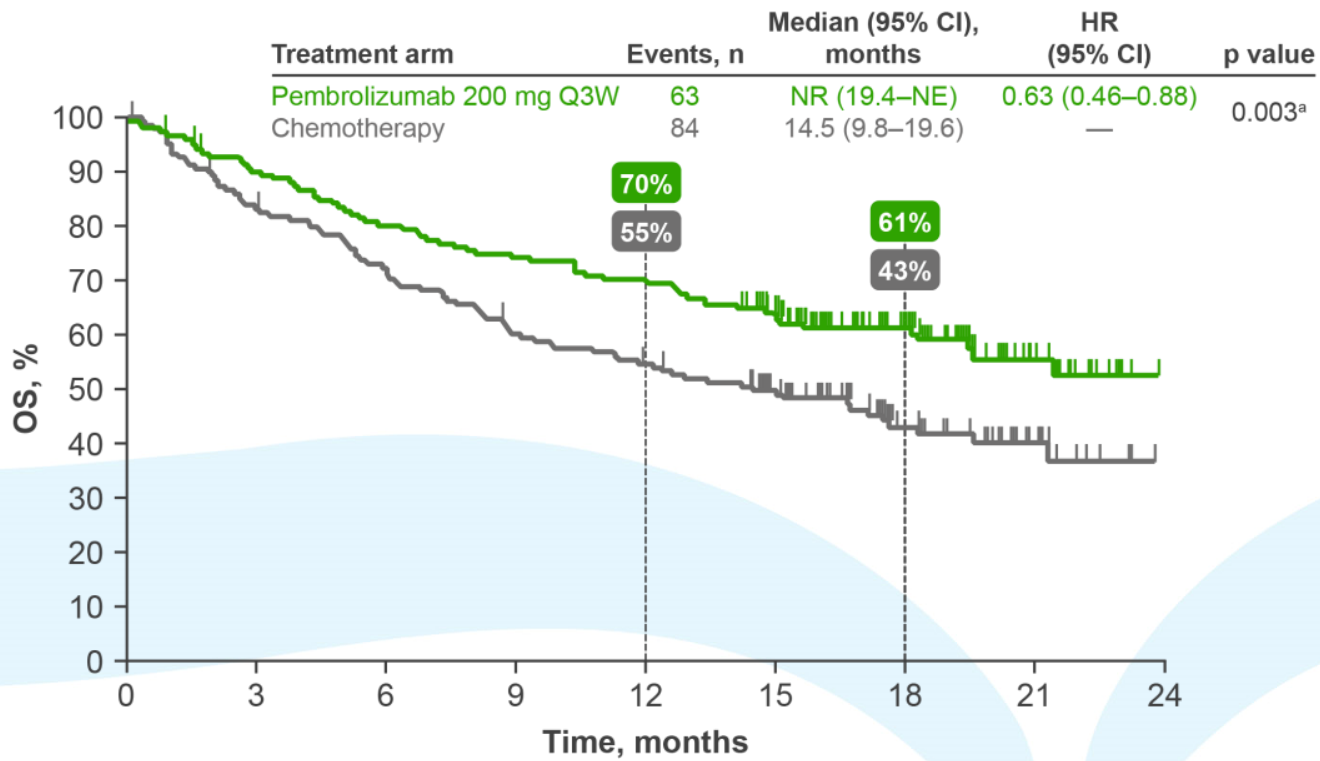
Patients
- Untreated stage IV NSCLC
- PD-L1 TPS ≥50%
- ECOG PS 0-1
- No sensitising *EGFR* mutation or *ALK* translocation
- No untreated brain metastases
- No active autoimmune disease requiring systemic therapy
- No active immune ILD or pneumonitis requiring systemic therapy

Key endpoints:
- Primary: PFS (RECIST v1.1 per blinded, independent central review)
- Secondary: OS, ORR, safety
- Exploratory: DOR



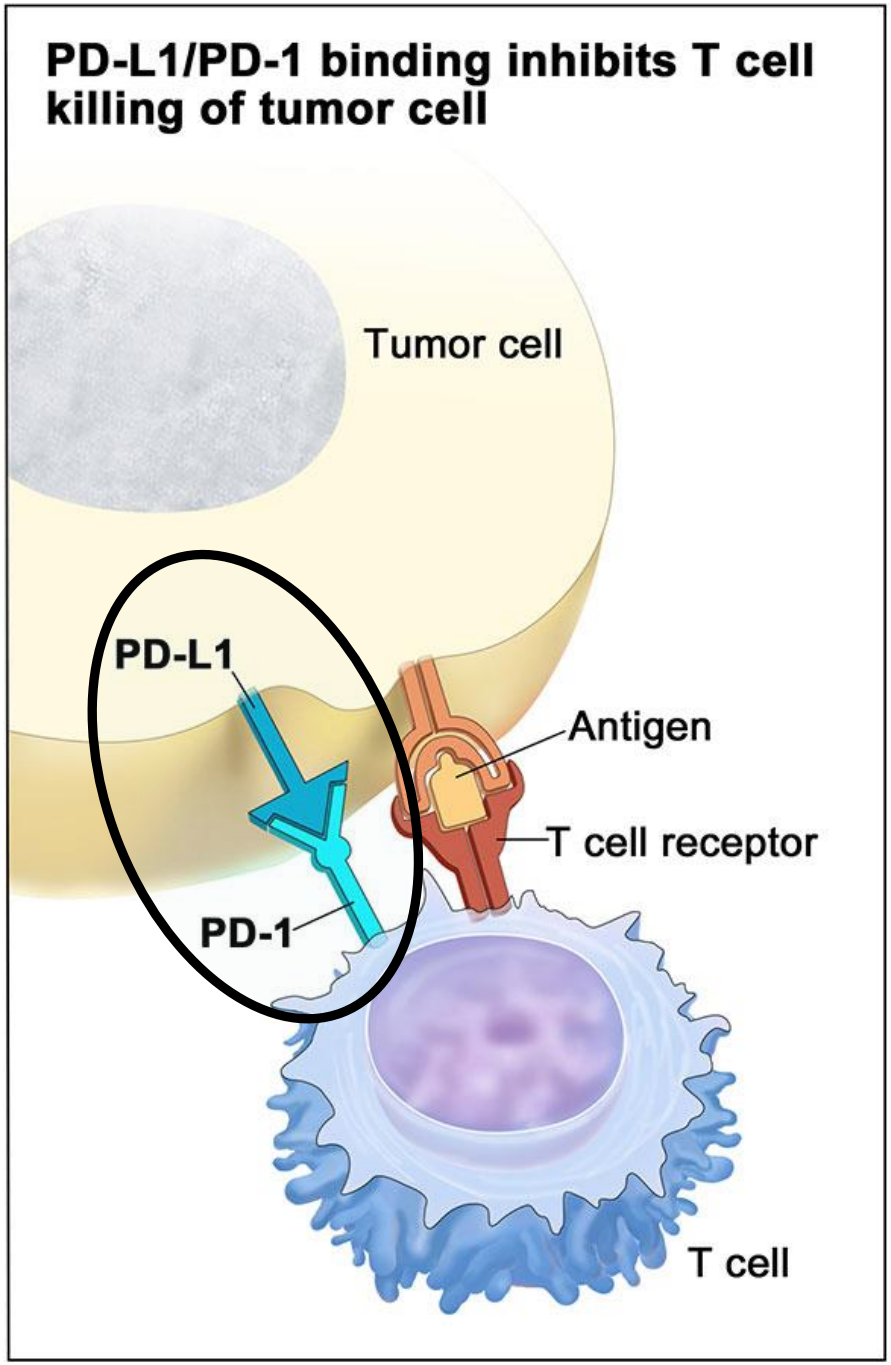
KEYNOTE-024: Pembrolizumab *vs.* **1st line** chemotherapy in non-small-cell lung cancer

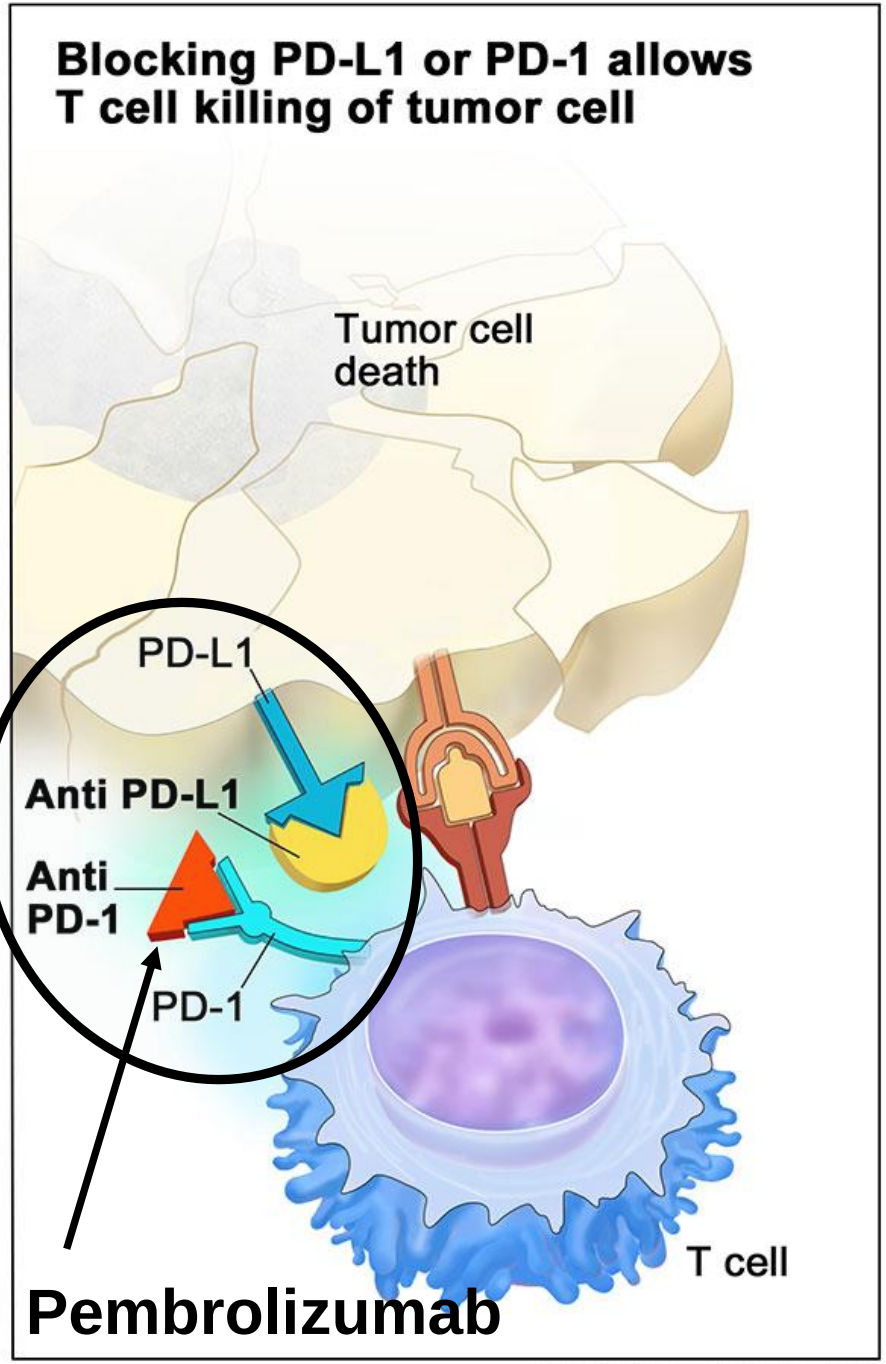
PD-L1 TPS>50%



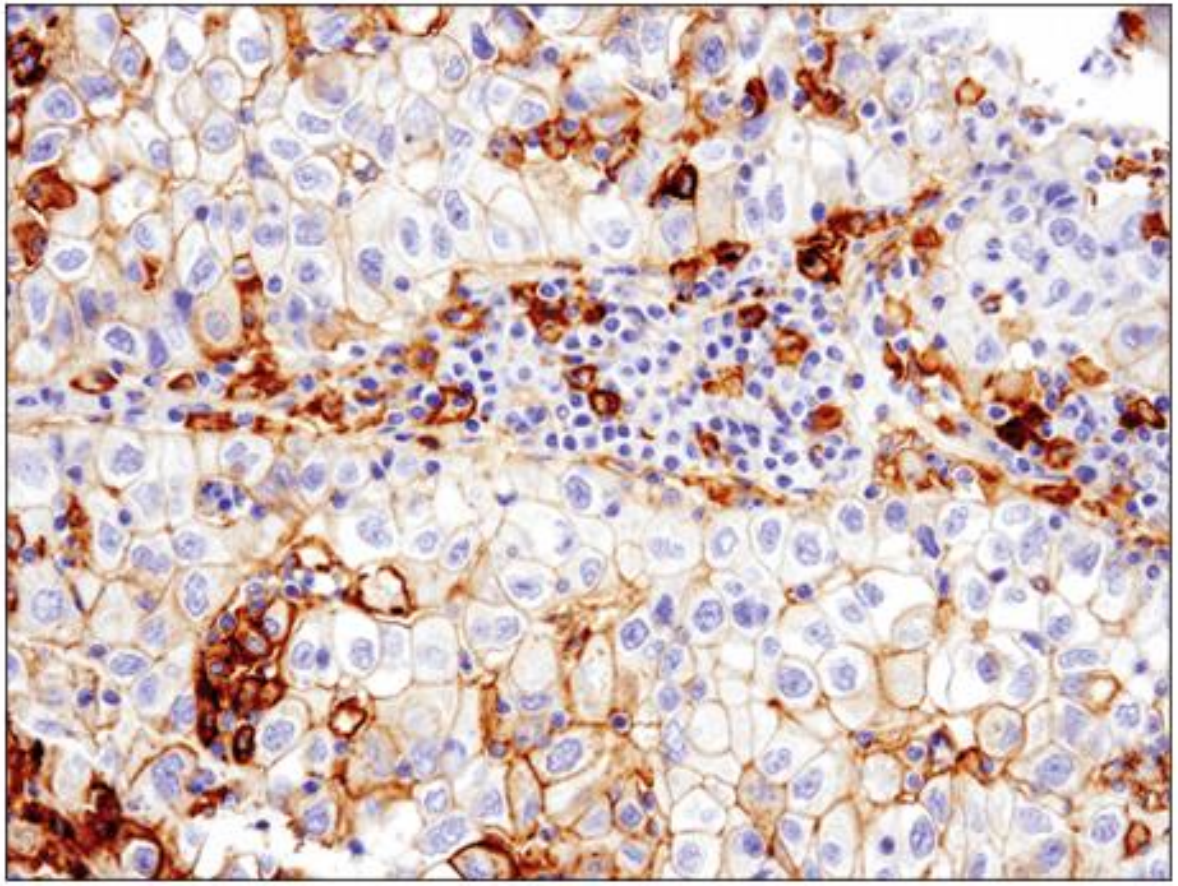
No. at risk									
Pembrolizumab 200 mg Q3W	154	136	121	112	106	88	57	20	4
Chemotherapy	151	123	107	88	79	64	35	15	4

What?





PDL-1 Detection



How?
(There are a number of different How’s)

Immuno-histochemical Antibody Testing

- Patient specimen and type
- An antibody
- Funding and costing
- Staff to carry out the test
- Consultant pathologists to read the test slides and report them
- The appropriate machine
- Validation(the easiest part)

Samples

There are lots of Ab's for PDL1

Antibody	Dako 22C3[1]	Dako 28-8[1]	Ventana SP142[1,2]	Ventana SP263[3]
Relevant expression	TC membrane	TC membrane	TCs + tumour-infiltrating ICs	TC membrane
Percentage expression for 'positivity' for licensed agents in advanced NSCLC*	≥1% or ≥50% For pembrolizumab*	≥1%, ≥5% and ≥10% For nivolumab[4-6*]	**n/a**	≥1% or ≥50% For pembrolizumab* ≥1, ≥5 and ≥10 For nivolumab[4-6*]

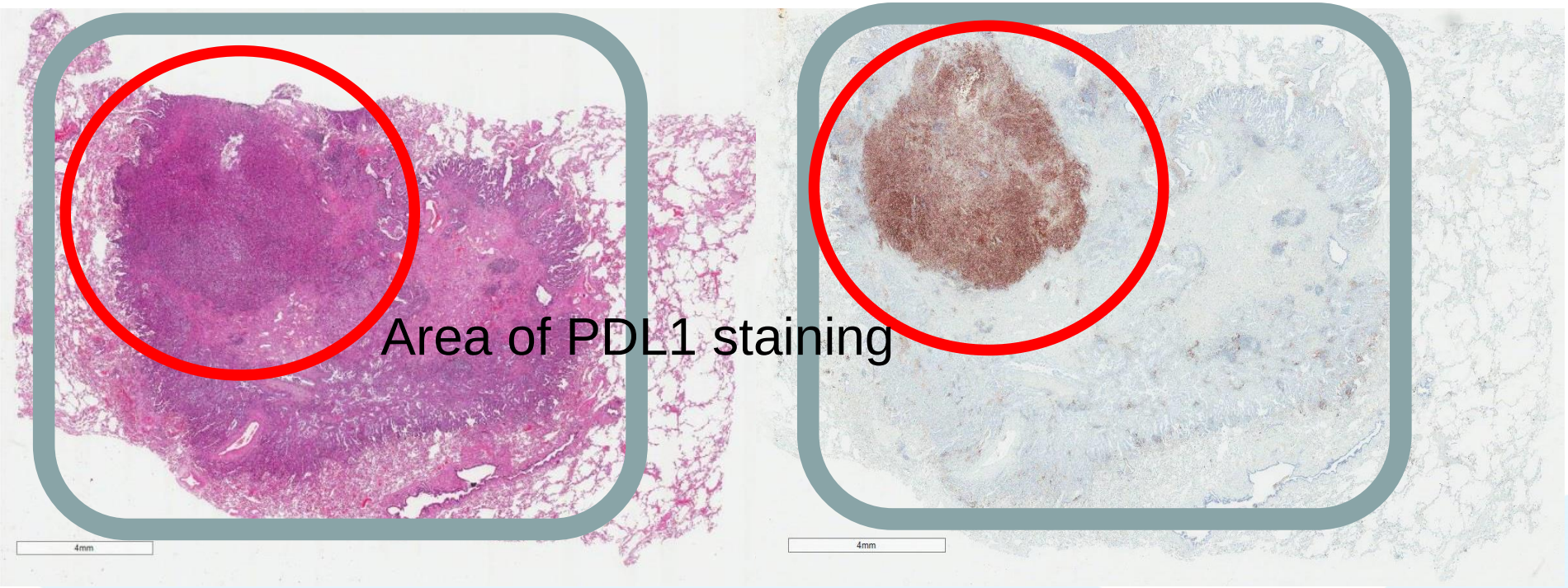
- Dako 28-8, Dako 22C3 and Ventana SP263 yield similar results for expression on tumour cells, but there appears to be variability for immune cell staining
- Ventana SP142 exhibited fewer stained tumour cells compared to the other three assays

Funding and Costing

- Molecular Pathology Evaluation Panel
- Scottish Pathology Network (SPAN)
- National costing agreed
- Sharing of information and business cases across the 3 regions

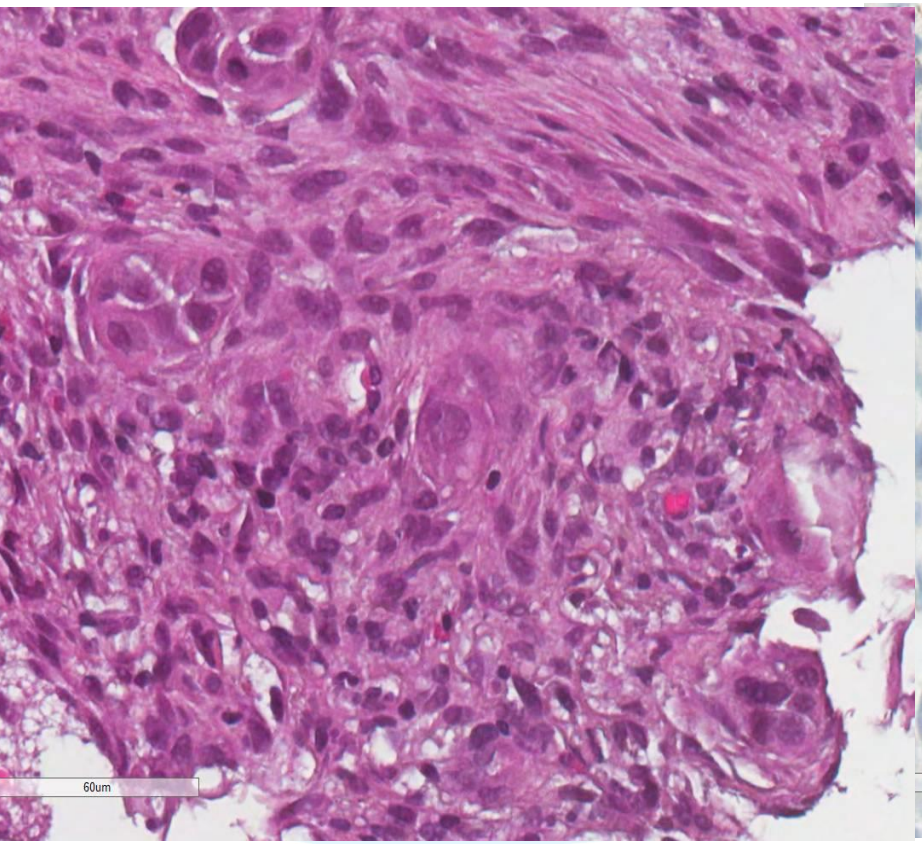
Getting the Machine and The Managed Service Contract

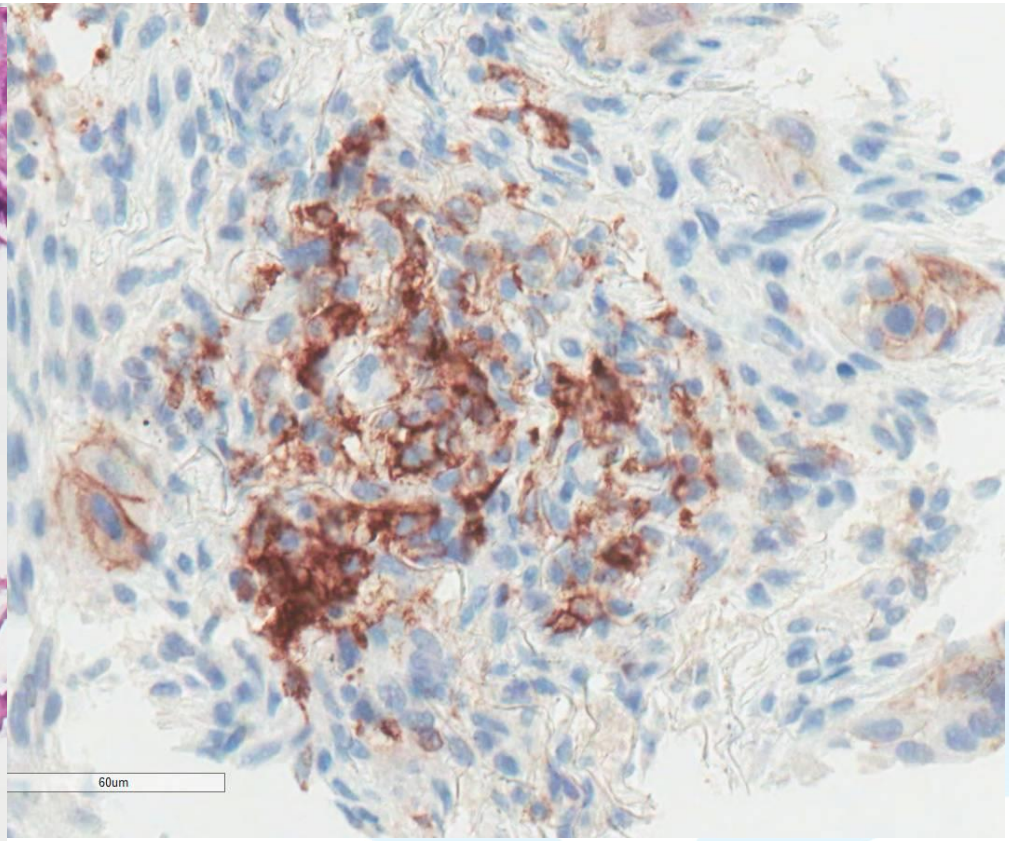
Reading the Test



Whole tumour area

Reading the Test





Testing Approach
Reflex, not Directed

Advantages

Saves time, both the patient's and the consultant's.

Provides clinicians with comprehensive information.

Permits forward planning.

Aids integration of information.

Disadvantages

Initial costs are higher.

Information might not be of immediate relevance.

Information might not be appropriate as the disease evolves.

How is this going?