WHAT'S NEXT IN BREAST CANCER BIOMARKER TESTING?

EXPLORING THE POTENTIAL OF PD-L1 AS A BIOMARKER IN TRIPLE-NEGATIVE BREAST CANCER

PD-L1=programmed death-ligand 1.

ROCHE: AT THE FOREFRONT OF BIOMARKER RESEARCH IN BREAST CANCER FOR MORE THAN 20 YEARS[1]

At Roche, we are committed to constantly improving outcomes for breast cancer patients

- Roche has pioneered the development of anti-HER2 breast cancer treatments and the HER2 companion diagnostic

TESTING FOR BIOMARKERS DRIVES BREAST CANCER CLASSIFICATION AND FIRST-LINE TREATMENT DECISIONS FOR METASTATIC DISEASE[2]

	ER+/PR+[2,3]	HER2+[2,4]	TNBC[2,3]
TEST	Positive expression confirmed by IHC	Positive expression confirmed by IHC or ISH	Confirmed ER-negative, PR-negative, and HER2-negative
PREVALENCE	Approximately 70% of invasive breast cancers	Approximately 15% of invasive breast cancers	Approximately 15% of invasive breast cancers
PROGNOSIS	• Less aggressive subtype • Fair prognosis with availability of hormonal therapies	• Aggressive subtype • HER2-targeted therapy changed the natural course of the disease and improved a previously poor prognosis	• Very aggressive subtype • Prognosis is poor, in part because patients are ineligible for hormonal or targeted therapies

- BRCA mutations represent an actionable biomarker for a small subset of patients with metastatic breast cancer, with prevalence varying between ethnic groups across geographies[3,5,6]
- Additional pathways and mutations are also under investigation, including **PD-L1** and PIK3CA/AKT/PTEN[7]

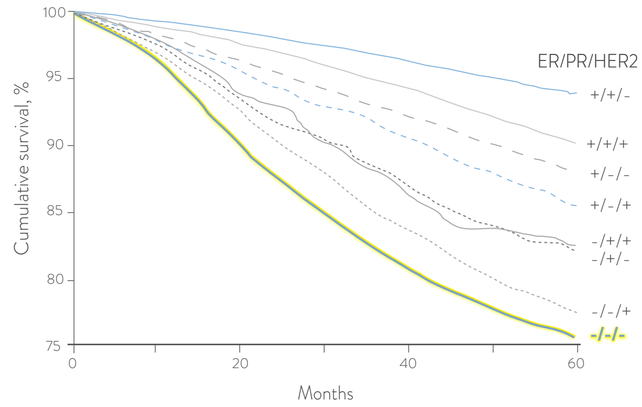
BRCA=breast cancer; ER=estrogen receptor; HER2=human epidermal growth factor receptor 2; IHC=immunohistochemistry; ISH=in situ hybridization; PIK3CA=enzymes also known as protein kinase B; PTEN=phosphatase and tensin homolog; PR=progesterone receptor; TNBC=triple-negative breast cancer.

TNBC REMAINS AN AREA OF SERIOUS UNMET NEED, CHARACTERISED BY A LACK OF VALIDATED PREDICTIVE BIOMARKERS[8,9]

TNBC is negative for ER, PR, and HER2 expression, making patients ineligible for therapies that target these biomarkers[2,3]

- TNBC is a heterogeneous, aggressive tumour subtype, accounting for ≈15% of invasive breast cancers[2]
- Chemotherapy is the current standard of care[3]

TNBC is characterised by shorter overall survival relative to HER2+ and HR+ breast cancer[10-11]



Kaplan-Meier graph illustrating relative 5-year patient survival by tumour type, according to time after treatment. Data are derived from diagnosis of mostly early breast cancer.

HR=hormone receptor.

LOWER MEDIAN OVERALL SURVIVAL

OS is lower in metastatic TNBC vs the general metastatic breast cancer population[12]:

13 MONTHS VS 2 TO 3.5 YEARS

PD-L1 IS A PROMISING BIOMARKER UNDER INVESTIGATION IN TNBC

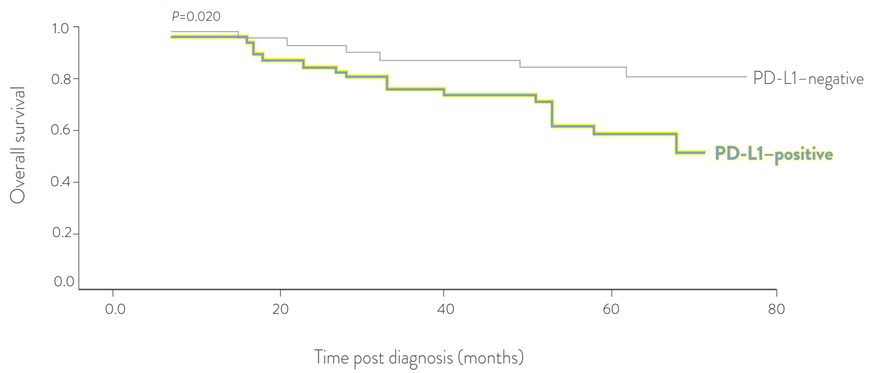
Elevated PD-L1 expression may be associated with poor prognosis in TNBC[13,14]

- Elevated PD-L1 expression may be associated with reduced survival in breast cancer[13,14]

RISK OF DEATH IS MORE THAN 2 TIMES HIGHER

IN PATIENTS WITH PD-L1–POSITIVE DISEASE compared with patients with PD-L1–negative disease (*P*<0.046)*

*Multivariate analysis adjusted by age, tumour size, grade, and lymph node status.

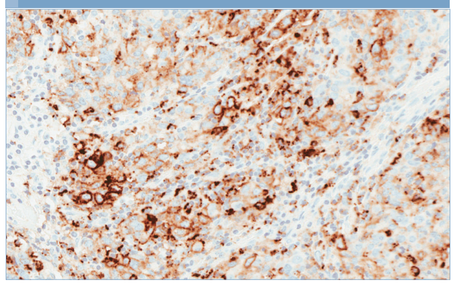


Kaplan-Meier survival curve for overall survival, depending on the expression of PD-L1 for basal-like breast cancer (ER-, PR-, HER2-).
P value calculated by the log-rank test.

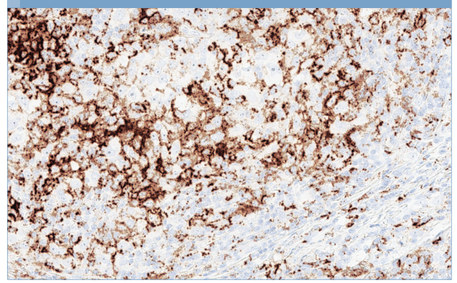
PD-L1 EXPRESSION IS ELEVATED IN TNBC RELATIVE TO OTHER TYPES OF BREAST CANCER[15]

- PD-L1 expression is elevated in TNBC compared with HR-positive disease and HER2-positive disease[15]
- PD-L1 can be expressed on both tumour cells and tumour-infiltrating immune cells, with status determined by IHC using different scoring methods and definitions of positivity[16,17]

PD-L1 ON TUMOUR CELLS



PD-L1 ON TUMOUR-INFILTRATING IMMUNE CELLS

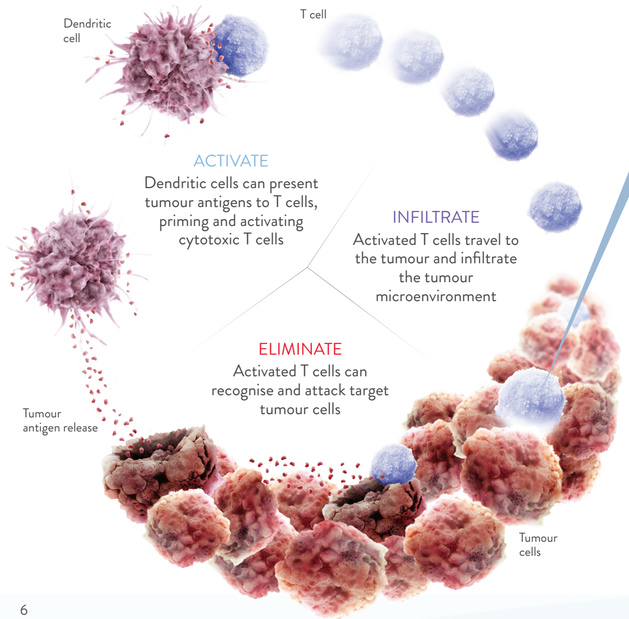


PD-L1 IS EASILY DETECTABLE ON IMMUNE CELLS IN TNBC[9,16,17]

PD-L1 IS ONE OF THE PRIMARY IMMUNOSUPPRESSIVE DRIVERS IN MULTIPLE TYPES OF CANCER

PD-L1 can suppress the cancer immunity cycle, which governs the immune response against cancer[16-19]

- The cancer immunity cycle is a scientific framework that describes how the immune system recognises and eradicates cancer

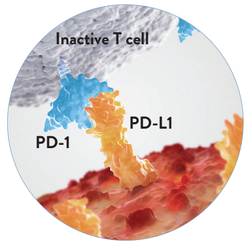


PD-L1

can disrupt the cancer immunity cycle by inhibiting T cells from killing tumour cells

PD-L1 is an inhibitory ligand expressed on tumour cells and infiltrating immune cells[16,17,19]

- PD-L1 binds to its receptor, PD-1, deactivating cytotoxic T cells
  - Once deactivated, T cells remain inhibited in the tumour microenvironment



IDENTIFYING PD-L1 ON TUMOUR *AND* IMMUNE CELLS MAY BE AN IMPORTANT CONSIDERATION FOR CANCER IMMUNOTHERAPY RESEARCH

Targeting PD-L1 on tumour cells and tumour-infiltrating immune cells may invigorate antitumour T-cell activity[16,18,20,21]

- Preventing PD-L1 from binding to PD-1 may invigorate suppressed T cells to kill tumour cells in the tumour microenvironment

MHC=major histocompatibility complex; PD-1=programmed death-1; TCR=T-cell receptor.

BRINGING A PASSION FOR PERSONALISED HEALTHCARE TO TNBC

Exploring PD-L1 as a biomarker may lead to more individualised treatment approaches for TNBC[18,22]

- **Metastatic TNBC is an area of high unmet need without validated biomarkers[8,9]**
  - An aggressive breast cancer subtype associated with poor survival outcomes[2,13,14]
- **The PD-L1 pathway represents a promising area of research in TNBC[17-19]**
  - PD-L1 expression is elevated in TNBC relative to other breast cancer subtypes[15]
  - Elevated PD-L1 expression may increase mortality in TNBC[12-14]

As part of our commitment to breast cancer and personalised healthcare, Roche is actively researching PD-L1 as a biomarker in TNBC

To learn more about PD-L1 and its status as a biomarker, visit
ResearchCancerImmunotherapy.com

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