oncovalue

Implementing value-based oncology care
at European cancer hospitals

case study

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ONCOVALUE - Implementing value-based oncology care at European cancer hospitals
This project has received funding from the European Union's Horizon Europe research and innovation programme under grant agreement No 101095245

Consortium of cancer centers & technology companies

Project duration: 1.12.2022 – 30.11.2026, 7 M€ total budget

HORIZON-HLTH-2022-TOOL-11-02: New methods for the effective use of real-world data and/or synthetic data in regulatory decision-making and/or in health technology assessment

HUS Helsinki University Hospital

Netherlands Cancer Institute – Antoni van Leeuwenhoek

Rijnstate

Region H – Rigshospitalet

IPO Porto – Instituto Português de Oncologia do Porto FG, EPE

Istituto Romagnolo per lo Studio dei Tumori Dino Amadori

Siemens Healthineers

BC Platforms

elevate

TTOPSTART

IQVIA™

CiaoTech

ONCOVALUE will

A. enable and guide **cancer hospitals to collect**, **harmonize** and **analyze** high quality RWD in **real-time**
   - *How to organize and maintain data collection as part of standard clinical routines?*
   - *How to harmonize hospital data sources (clinical, quality-of-life and costs data) to enable federated analytics?*

B. empower and train **regulatory** and **HTA-bodies** to **adopt** RWD-driven methodologies **in their decision-making on cost-effectiveness of novel cancer therapies**.
   - *Real-life clinical use cases on targeted therapies for breast cancer and non-small-cell lung cancer*
   - *Pilot studies on feasibility, data quality, and federated data access tools*
   - *Educational content*

C. develop and test next generation **AI-based tools supporting the effective use of unstructured data**
   - *Text analytics to extract and structure clinical information (oncologist's evaluation of treatment response and adverse events) from free text.*
   - *Detection and analysis of response to treatment (disease progression vs. clinical benefit) from CT scans of the metastatic target lesions.*

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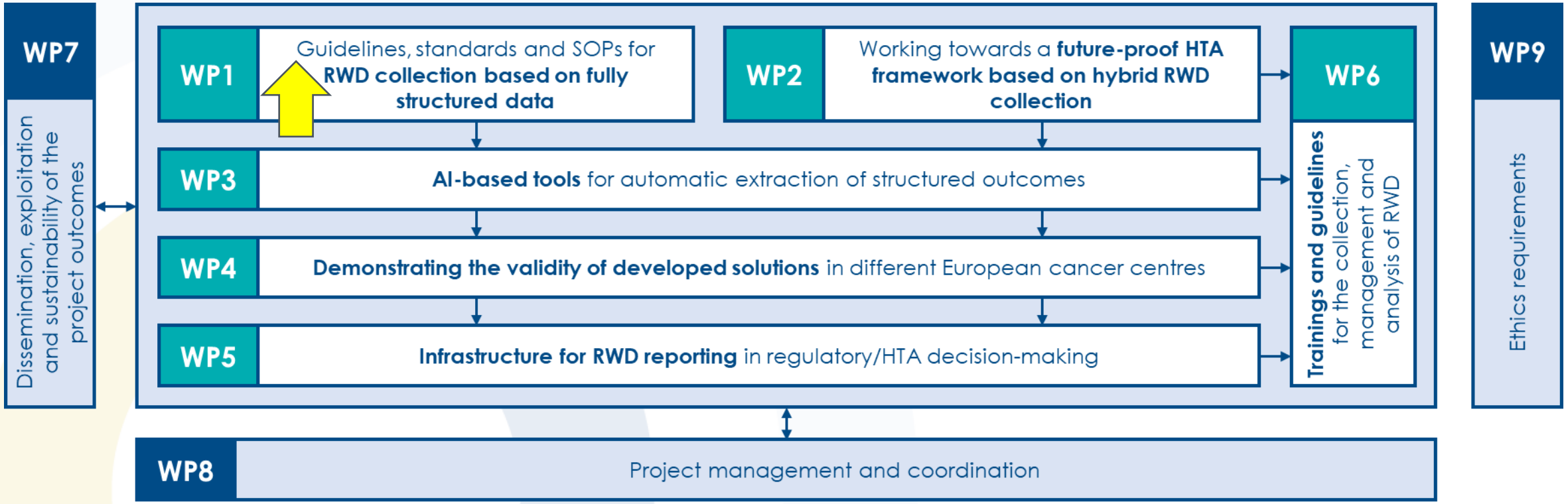
Work packages (WP)



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Use case / HUS

- EMA 4/2022: **Pembrolizumab** in combination with chemotherapy as **neoadjuvant treatment**, and then continued as monotherapy as **adjuvant treatment** after surgery, is indicated for the treatment of adults **with locally advanced, or early stage triple negative breast cancer (TNBC) at high risk of recurrence**.

- In Finland at HUS 12/2022

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Use case / HUS

- Pembrolizumab in the neoadjuvant and adjuvant treatment of Triple-Negative Breast Cancer

1. *Schmid P. et al New England Journal of Medicine 2020*
   - patient and tumor characteristics
   - pCR (pathologic complete response)
   - safety (adverse events)

2. *Schmid P. et al New England Journal of Medicine 2022*
   - event free survival

3. *Not yet published*
   - overall survival

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The NEW ENGLAND JOURNAL of MEDICINE 2020

ORIGINAL ARTICLE

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Table 1. Characteristics of the Patients at Baseline.*

Characteristic	Pembrolizumab–Chemotherapy (N=784)	Placebo–Chemotherapy (N=390)
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Premenopausal	438 (55.9)	221 (56.7)
Postmenopausal	345 (44.0)	169 (43.3)
PD-L1 status — no. (%)†		
Positive	656 (83.7)	317 (81.3)
Negative	127 (16.2)	69 (17.7)
ECOG performance-status score — no. (%)‡		
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1	106 (13.5)	49 (12.6)
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Stage II	590 (75.3)	291 (74.6)
Stage III	194 (24.7)	98 (25.1)
HER2 status score — no. (%)§		
0–1	595 (75.9)	286 (73.3)
2+	188 (24.0)	104 (26.7)

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- patient characteristics
  - age
  - menopause status
  - ECOG status

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patient characteristics

- Patients n=58
- age
  - median age 50.5 (range 20 - 78)
  - <65 years n=46 (79%)
- menopausal status
  - premenopausal n= 26 (45%)
  - postmenopausal n= 29 (50%)
  - NA n= 3(5%)
- ECOG status
  - 0 n=23 (35%)
  - 1 n=1 (3%)
  - NA n=34 (59%)

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- tumor characteristics
  - PDL-1 status
  - Primary tumor at baseline
  - Nodal involvement
  - HER2 status score

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tumor characteristics

- T at baseline
  - T0 n=2 (3%)
  - T1-T2 n=48 (83%)
  - T3-T4 n=6 (10%)
  - NA n=3 (4%)
- Nodal involvement
  - Positive n=28 (48%)
  - Negative n=28 (48%)
  - NA n=2 (3%)
- HER-2 status score
  - 0-1+ n=44 (76%)
  - 2+ n=7 (12%)
  - NA n=7 (12%)

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safety

- ONCOVALUE: No toxic deaths
- n=13 pts interrupted the treatment due to adverse events
  - IO-adverse events n=11 (hepatitis, hypo/hyperthyreoidism, myocarditis, adrenal insufficiency, skin reaction)
  - Neutropenic sepsis n=1
  - Renal failure n=1

Table 3. Adverse Events during the Neoadjuvant Phase at the Second Interim Analysis.*

Event	Pembrolizumab–Chemotherapy (N=781)		Placebo–Chemotherapy (N=389)	
	Any Grade	Grade ≥3	Any Grade	Grade ≥3
	number of patients (percent)			
Any adverse event	777 (99.5)	633 (81.0)	389 (100.0)	295 (75.8)
Treatment-related adverse event†	773 (99.0)	600 (76.8)	388 (99.7)	281 (72.2)
Nausea	490 (62.7)	26 (3.3)	246 (63.2)	5 (1.3)
Alopecia	471 (60.3)	14 (1.8)	220 (56.6)	8 (2.1)
Anemia	430 (55.1)	142 (18.2)	215 (55.3)	58 (14.9)
Neutropenia	365 (46.7)	270 (34.6)	183 (47.0)	129 (33.2)
Fatigue	321 (41.1)	27 (3.5)	147 (37.8)	6 (1.5)
Diarrhea	230 (29.4)	17 (2.2)	92 (23.7)	5 (1.3)
Elevated alanine aminotransferase level	199 (25.5)	41 (5.2)	96 (24.7)	9 (2.3)
Vomiting	199 (25.5)	18 (2.3)	85 (21.9)	6 (1.5)
Asthenia	191 (24.5)	25 (3.2)	99 (25.4)	9 (2.3)
Constipation	185 (23.7)	0	82 (21.1)	0
Decreased neutrophil count	185 (23.7)	146 (18.7)	112 (28.8)	90 (23.1)
Rash	170 (21.8)	7 (0.9)	59 (15.2)	1 (0.3)
Peripheral neuropathy	154 (19.7)	15 (1.9)	82 (21.1)	4 (1.0)
Adverse event of interest‡	304 (38.9)	101 (12.9)	71 (18.3)	7 (1.8)
Infusion reaction	132 (16.9)	20 (2.6)	43 (11.1)	4 (1.0)
Hypothyroidism	107 (13.7)	3 (0.4)	13 (3.3)	0
Hyperthyroidism	36 (4.6)	2 (0.3)	4 (1.0)	0
Severe skin reaction	34 (4.4)	30 (3.8)	4 (1.0)	1 (0.3)
Adrenal insufficiency	18 (2.3)	10 (1.3)	0	0

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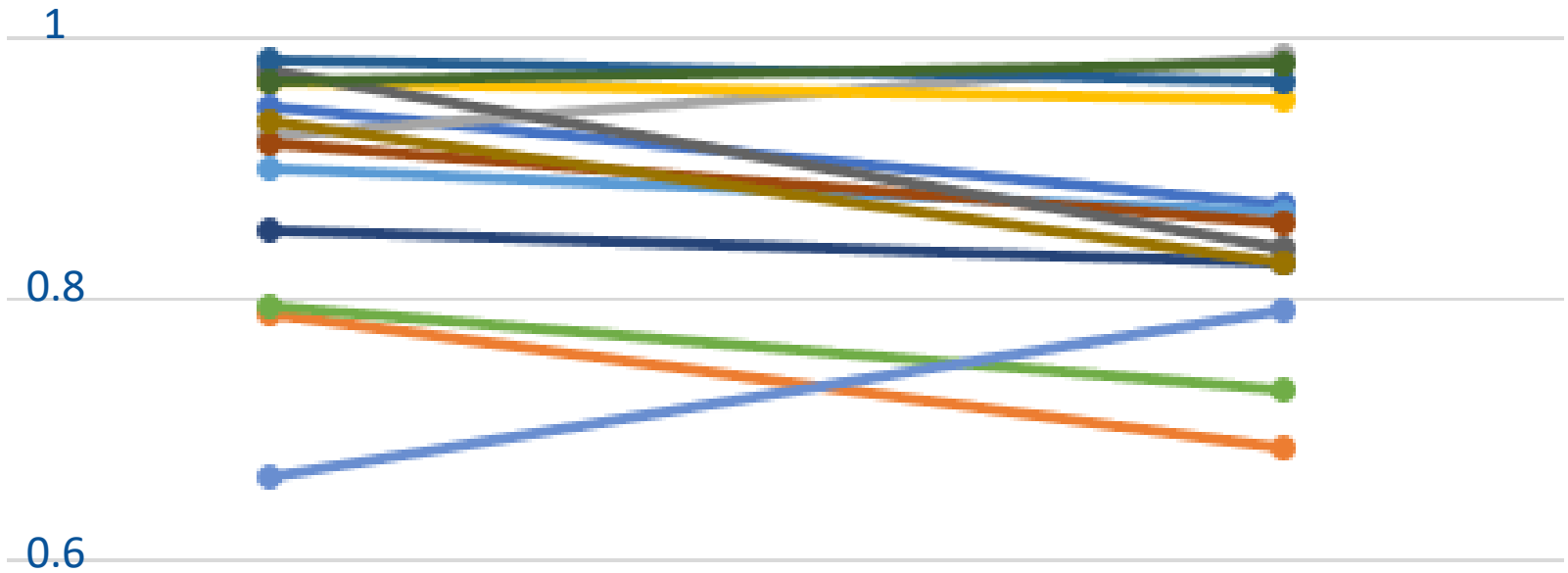
quality of life

- QoL at baseline compared to ~6 moths (the timepoint nearest to the 6 monts between 4 and 8 months). N=12 patients. Average index change -0.03 index points.



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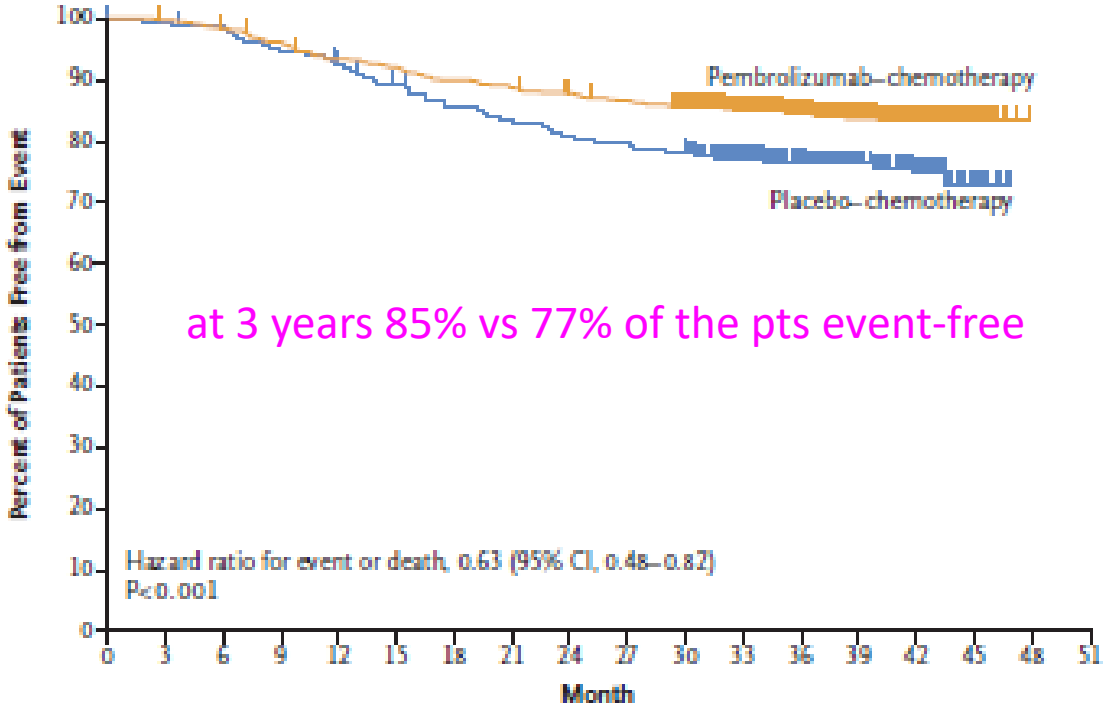
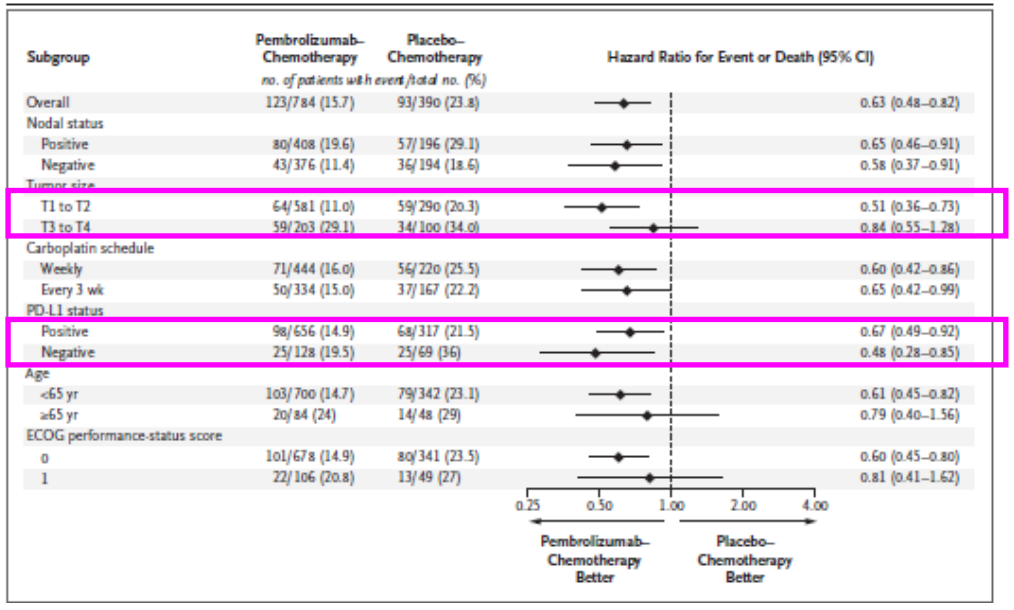
Use case / HUS



at 3 years 85% vs 77% of the pts event-free

No. at Risk

Pembrolizumab–chemotherapy	784	781	769	751	728	718	702	692	681	671	652	551	433	303	165	28	0	0
Placebo–chemotherapy	390	386	382	368	358	342	328	319	310	304	297	250	195	140	83	17	0	0



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The authors' full names, academic degrees, and affiliations are listed in the Appendix. Dr. Schmid can be contacted at p.schmid@qmul.ac.uk or at the Centre of Experimental Cancer Medicine, Barts Cancer Institute, Queen Mary University of London, Old Anatomy Bldg., Charterhouse Sq., London EC1M 6BQ, United Kingdom.

*The complete list of investigators in the KEYNOTE-522 trial is provided in the Supplementary Appendix, available at NEJM.org.

N Engl J Med 2022;386:556-67.
DOI: 10.1056/NEJMoa2112651

ABSTRACT

BACKGROUND
The addition of pembrolizumab to neoadjuvant chemotherapy led to a significantly higher percentage of patients with early triple-negative breast cancer having a pathological complete response (defined as no invasive cancer in the breast and negative nodes) at definitive surgery in an earlier analysis of this phase 3 trial of neoadjuvant and adjuvant therapy. The primary results regarding event-free survival in this trial have not been reported.

METHODS
We randomly assigned, in a 2:1 ratio, patients with previously untreated stage II or III triple-negative breast cancer to receive neoadjuvant therapy with four cycles of pembrolizumab (at a dose of 200 mg) or placebo every 3 weeks plus paclitaxel and carboplatin, followed by four cycles of pembrolizumab or placebo plus doxorubicin–cyclophosphamide or epirubicin–cyclophosphamide. After definitive surgery, patients received adjuvant pembrolizumab (pembrolizumab–chemotherapy group) or placebo (placebo–chemotherapy group) every 3 weeks for up to nine cycles. The primary end points were pathological complete response (the results for which have been reported previously) and event-free survival, defined as the time from randomization to the date of disease progression that precluded definitive surgery, local or distant recurrence, occurrence of a second primary cancer, or death from any cause. Safety was also assessed.

RESULTS
Of the 1174 patients who underwent randomization, 784 were assigned to the pembrolizumab–chemotherapy group and 390 to the placebo–chemotherapy group. The median follow-up at this fourth planned interim analysis (data cutoff, March 25, 2021) was 39.1 months. The estimated event-free survival at 36 months was 84.5% (95% confidence interval [CI], 81.7 to 86.9) in the pembrolizumab–chemotherapy group, as compared with 76.8% (95% CI, 72.2 to 80.7) in the placebo–chemotherapy group (hazard ratio for event or death, 0.63; 95% CI, 0.48 to 0.82; P<0.001). Adverse events occurred predominantly during the neoadjuvant phase and were consistent with the established safety profiles of pembrolizumab and chemotherapy.

CONCLUSIONS
In patients with early triple-negative breast cancer, neoadjuvant pembrolizumab plus chemotherapy, followed by adjuvant pembrolizumab after surgery, resulted in significantly longer event-free survival than neoadjuvant chemotherapy alone. (Funded by Merck Sharp and Dohme, a subsidiary of Merck; KEYNOTE-522 ClinicalTrials.gov number, NCT03036488.)

- event-free survival
  - event-free n=52 out of 58 (90%) after the median follow-up (13.1 months) of the present Oncovalue analysis
  - in the future % event free at 1, 2, 3 years
- overall survival
  - alive n=54 out of 58 (93%) after the median follow-up (13.1 months) of the present Oncovalue analysis
  - in the future % alive at 1,2 3 years

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Use case / technical solutions for data

Pembrolizumab in the Neoadjuvant and Adjuvant Treatment of Triple-Negative Breast Cancer

- The data extraction logic was built in the HUS Datalake by HUS data analysts
- Clinicians and medical students have supported by consulting and validating the data

Main data sources

- EPIC EMR: Diagnosis, demographics, medications, procedures, QALYs, patient texts
- My+ pathology system: Pathological data
- Multilab: Labs

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Identification of the non-responders vs. best responders

- **Clinical and tumor biologic characterisation** of the non-responders vs. best responders
  - **Continuous collection of bio-banking specimens** by informing all new patients by a study nurse on the possibility to give the Helsinki bio-banking sample after consent.
- Capabilities for **automated collection of structured real world clinical data** is being built in the whole breast cancer patient path
- The concept will be copied to other tumor types as well

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Thank you!

www.oncovalue.org

https://www.linkedin.com/company/oncovalue/