An Update on Clinical and Translational Research in Breast Cancer

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Disclosures

- **Research Funding**: Celgene, Corcept Therapeutics, Merck
- **Consultant or advisory role**: AstraZeneca, Celgene, Genentech, Immunomedics, Merck, Pfizer, Puma Biotechnology, Syndax
- **Data Safety Monitoring Board**: G1 Therapeutics
Agenda

• Targeting HER2 in Early Breast Cancer
• CDK 4/6 Inhibitors
• PARP Inhibitors
• Anti-PD-1/PD-L1 Inhibitors
• Antibody Drug Conjugates
• Breast Cancer Trials open through the PCCC
## Neoadjuvant Pertuzumab/Trastuzumab

<table>
<thead>
<tr>
<th>Treatment</th>
<th>NEOSPHERE¹</th>
<th>TRYPHAENA²</th>
<th>TRYPHAENA²</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Treatment</strong></td>
<td>Pertuzumab, Trastuzumab, Docetaxel</td>
<td>Docetaxel/Carbo/Trastuzumab/Pertuzumab</td>
<td>Docetaxel/Carbo/Trastuzumab/Pertuzumab</td>
</tr>
<tr>
<td></td>
<td>THP x 4</td>
<td>TCHP x 6</td>
<td>FEC x 3 → THP x 3</td>
</tr>
<tr>
<td><strong>FEC x 3 post-op</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>N</strong></td>
<td>107</td>
<td>77</td>
<td>75</td>
</tr>
<tr>
<td><strong>ypT0/is ypN0 (%)</strong></td>
<td>39.3</td>
<td>63.6</td>
<td>54.6</td>
</tr>
</tbody>
</table>

- NEOSPHERE AND TRYPHAENA led to accelerated approval in 9/2013
- Final approval to be determined by APHINITY

APHINITY: Randomized Adjuvant Phase 3 Trial

N=3800 planned (4800 enrolled)

Central confirmation of HER2 status

Population: Node + or high risk node negative

ACT or TCH
trastuzumab + pertuzumab* x 1 year

ACT or TCH
trastuzumab + placebo* x 1 year

*antibody therapy starts with taxane

A=doxorubicin, E=epirubicin, C=cyclophosphamide, T=taxane (paclitaxel or docetaxel), F=5-fluorouracil, H=trastuzumab, P=pertuzumab

Von Minckwitz et al. ASCO 2017 Abs LBA500
APHINITY: Disease-Free Survival

4yr iDFS:
HR = 0.81 (p = 0.045)
Absolute benefit = 1.7%

iDFS subset analysis

<table>
<thead>
<tr>
<th></th>
<th>Δ % (H/P vs. H)</th>
<th>Absolute Δ</th>
</tr>
</thead>
<tbody>
<tr>
<td>N0</td>
<td>96.7 v 96.2%</td>
<td>0.5%</td>
</tr>
<tr>
<td>N1</td>
<td>89.9 v 86.7%</td>
<td>3.2%</td>
</tr>
<tr>
<td>ER/PR+</td>
<td>93 v 91.6%</td>
<td>1.4%</td>
</tr>
<tr>
<td>ER/PR-</td>
<td>91 v 88.7%</td>
<td>2.3%</td>
</tr>
</tbody>
</table>

*No difference in iDFS by type of chemotherapy

von Mickwitz G et al, ASCO 2017
Primary endpoint: invasive disease-free survival (iDFS)\textsuperscript{a}

Secondary endpoints: overall survival, DFS-DCIS, distant DFS, time to distant recurrence, CNS metastases, safety,

Stratification: nodes 0, 1-3 vs 4+, ER/PR status, concurrent vs sequential trastuzumab

Study blinded: Until primary analysis; OS remains blinded

\textsuperscript{a} All iDFS events up to the cutoff date of 2 years + 28 days for each patient were included in the primary analysis.
5-year Analysis Shows Durable iDFS Benefit

ITT Population

Neratinib FDA-approved for extended adjuvant treatment of early stage HER2+ breast cancer (July 17, 2017)

HR (95% CI): 0.73 (0.57-0.92)
Two-sided P=0.008

At risk

<table>
<thead>
<tr>
<th>Months after randomization</th>
<th>0</th>
<th>12</th>
<th>24</th>
<th>36</th>
<th>48</th>
<th>60</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neratinib</td>
<td>1420</td>
<td>1316</td>
<td>1272</td>
<td>1225</td>
<td>1106</td>
<td>978</td>
</tr>
<tr>
<td>Placebo</td>
<td>1420</td>
<td>1354</td>
<td>1298</td>
<td>1248</td>
<td>1142</td>
<td>1029</td>
</tr>
</tbody>
</table>

(Descriptive P value)
iDFS by Hormone Receptor Status

5-Year Analysis

Hormone receptor positive

Hormone receptor negative

Disease-free survival

At risk

At risk

Neratinib 816 757 731 705 642 571 565 558 554 544 523

Placebo 815 779 750 719 647 581 567 556 551 542 525

Neratinib 816 757 731 705 642 571 565 558 554 544 523

Placebo 815 779 750 719 647 581 567 556 551 542 525

Martin M ESMO 2017
Crosstalk between ER/PR and CDK4/6 pathway in BC

- Imbalance of the cyclin D and CDK pathway in cancer cells may result in a more proliferative phenotype
- ER+ breast cancer may have features suggesting particular dependence on the CDK4/cyclin D1/Rb interaction
  - Aberrations leading to hyperactivation of cyclin D1-CDK4/6 are particularly common in ER+ BC
PALOMA-2 & MonaLEEesa-2 & MONARCH-3
Progression-Free Survival

**PALOMA-2**

- 24.8 mo vs. 14.5 mo
- HR: **0.58** (0.46–0.72)

**MONALEESA-2**

- 25.3 vs 16 mos
- HR: **0.57** (0.43–0.72)

**MONARCH-3**

- NR vs 14.7 mo
- HR: **0.543** (0.409, 0.723)

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Palbociclib + fulvestrant (Paloma 3)
Abemaciclib monotx (Monarch-1)
PARP Inhibitors

- Talazoparib
- Niraparib
- Rucaparib
- Olaparib
- Veliparib

Potency: Highest to Lowest
OlympiAD study design

- HER2-negative metastatic BC
  - ER+ and/or PR+ or TNBC
- Deleterious or suspected deleterious gBRCAm
- Prior anthracycline and taxane
- ≥2 prior chemotherapy lines in metastatic setting
- HR+ disease progressed on ≥1 endocrine therapy, or not suitable
- If prior platinum use
  - No evidence of progression during treatment in the advanced setting
  - ≥12 months since (neo)adjuvant treatment

Primary endpoint:
- Progression-free survival (RECIST 1.1, BICR)

Secondary endpoints:
- Time to second progression or death
- Overall survival
- Objective response rate
- Safety and tolerability
- Global HRQoL (EORTC-QLQ-C30)

Treatment:
- Olaparib 300 mg tablets bd
- 2:1 randomization
- Treat until progression

Chemotherapy treatment of physician’s choice (TPC)
- Capecitabine
- Eribulin
- Vinorelbine

BICR: blinded independent central review; ER, estrogen receptor; HRQoL, health-related quality of life; PR, progesterone receptor; RECIST, response evaluation criteria in solid tumors; TNBC, triple-negative breast cancer

Presented at:
ASCO ANNUAL MEETING '17 | #ASCO17
Presented by: Mark Robson, MD
6/4/2017
Primary endpoint: progression-free survival by BICR

- Olaparib 300 mg bd
- Chemotherapy TPC

<table>
<thead>
<tr>
<th></th>
<th>Olaparib 300 mg bd</th>
<th>Chemotherapy TPC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Progression/deaths, n (%)</td>
<td>163 (79.5)</td>
<td>71 (73.2)</td>
</tr>
<tr>
<td>Median PFS, months</td>
<td>7.0</td>
<td>4.2</td>
</tr>
<tr>
<td>HR</td>
<td>0.58</td>
<td></td>
</tr>
<tr>
<td>95% CI</td>
<td>0.43 to 0.80</td>
<td></td>
</tr>
<tr>
<td>P value</td>
<td>0.0009</td>
<td></td>
</tr>
</tbody>
</table>
EMBRACCA Study Design

Patients with locally advanced or metastatic HER2-negative breast cancer and a germline *BRCA1* or *BRCA2* mutation*†*

Stratification factors:
- Number of prior chemo regimens (0 or ≥ 1)
- TNBC or hormone receptor positive (HR+)
- History of CNS mets or no CNS mets

**Primary endpoint**
- Progression-free survival by RECIST by blinded central review

**Key secondary efficacy endpoints**
- Overall survival (OS)
- ORR by investigator
- Safety

**Exploratory endpoints**
- Duration of response (DOR) for objective responders
- Quality of life (QoL; EORTC QLQ-C30, QLQ-BR23)

Phase 3, international, open-label study randomized
431 patients in 16 countries and 145 sites
Primary Endpoint: PFS

<table>
<thead>
<tr>
<th></th>
<th>TALA (n = 287)</th>
<th>Overall PCT (n = 144)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Events, no. (%)</td>
<td>186 (65%)</td>
<td>83 (58%)</td>
</tr>
<tr>
<td>Median, mo (95% CI)</td>
<td>8.6 (7.2, 9.3)</td>
<td>5.6 (4.2, 6.7)</td>
</tr>
</tbody>
</table>

Hazard ratio, 0.54, 95% CI, 0.41, 0.71

P < .0001

No. at risk (events/cumulative events)

<table>
<thead>
<tr>
<th></th>
<th>TALA</th>
<th>Overall PCT</th>
</tr>
</thead>
<tbody>
<tr>
<td>TALA</td>
<td>287</td>
<td>144</td>
</tr>
<tr>
<td>PCT</td>
<td>144</td>
<td>144</td>
</tr>
</tbody>
</table>

PFS: Progression-free survival
Brightness Study Design

Study Objectives

Primary objectives:
• pCR

Secondary objectives:
• EFS, OS, breast conservation rate

Tertiary objectives:
• MRI, near pCR, QoL

Legend:
- First day of treatment with veliparib/placebo + carboplatin/placebo + paclitaxel
- Last dose of veliparib/placebo + carboplatin/placebo + paclitaxel

a Performed at least 2 weeks after last chemotherapy treatment.
b Surgery (+/- radiotherapy) was recommended approximately 2–8 weeks after last chemotherapy treatment.
Efficacy

- Addition of veliparib and carbo significantly improved pCR over control (53.2% vs 31.0%, \(p<0.001\)) confirming results of I-SPY-2.

- Addition of veliparib to carbo/paclitaxel did not demonstrate improvement in pCR compared to carbo/paclitaxel arm (53.2% vs 57.5%, \(p=0.36\)).

- Increase in pCR with addition of carboplatin was independent of gBRCA mutation status.

- No improvement in RFS/OS, but increased toxicity with the addition of carboplatin to standard T-AC neoadjuvant therapy.
# Anti-PD-1/PD-L1 Trials Reported to Date

<table>
<thead>
<tr>
<th>Agent</th>
<th>Subtype</th>
<th>ORR</th>
<th>ORR (PD-L1+)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Pembrolizumab</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Keynote-012</td>
<td>TNBC</td>
<td>18.5%</td>
<td>18.5%</td>
</tr>
<tr>
<td>• Keynote-028</td>
<td>ER+</td>
<td>12.0%</td>
<td>12.0%</td>
</tr>
<tr>
<td>• Keynote-086-A</td>
<td>TNBC</td>
<td>4.7%</td>
<td>4.8%</td>
</tr>
<tr>
<td><strong>Keynote-086-B (Frontline)</strong></td>
<td>TNBC</td>
<td><strong>23.0%</strong></td>
<td><strong>23.0%</strong></td>
</tr>
<tr>
<td><strong>Atezolizumab 1a</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• All</td>
<td>TNBC</td>
<td>10.0%</td>
<td>13.0%</td>
</tr>
<tr>
<td>• Frontline</td>
<td>TNBC</td>
<td><strong>26.0%</strong></td>
<td>NR</td>
</tr>
<tr>
<td><strong>Avelumab</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Single agent (Javelin)</td>
<td>All</td>
<td>4.8%</td>
<td>33.3% (4/12)</td>
</tr>
<tr>
<td></td>
<td>ER+</td>
<td>2.8%</td>
<td>NR</td>
</tr>
<tr>
<td></td>
<td>HER2+</td>
<td>3.8%</td>
<td>NR</td>
</tr>
<tr>
<td></td>
<td>TNBC</td>
<td>8.6%</td>
<td>44.4% (4/9)</td>
</tr>
</tbody>
</table>

*Studies used different antibodies and cutoffs for determining PD-L1 positivity*
Overall Survival by Best Response

Pembrolizumab single agent in mTNBC ≥1L, PDL1+/-

N=81
Median OS: 19.2 mo

Atezolizumab single agent in mTNBC ≥1L, PDL1+/-

1-y OS: 51%
1-y OS: 33%

Pembrolizumab single agent in mTNBC 1L, PDL1+

Atezolizumab 1a: OS by PD-L1 Status

Overall Survival

Time (months)

1-y OS: 45%
1-y OS: 37%
2-y OS: 28%
3-y OS: 28%

PD-L1 Status
- IC2/3 (n = 71)
- IC0/1 (n = 38)

Schmid et al, AACR 2017

<table>
<thead>
<tr>
<th>PD-L1 Status</th>
<th>All Pts (n = 113)</th>
<th>IC2/3 (n = 71)</th>
<th>IC0/1 (n = 38)</th>
</tr>
</thead>
<tbody>
<tr>
<td>mOS (95% CI)</td>
<td>9.3 mo (7.0, 12.6)</td>
<td>10.7 mo (7.2, 14.7)</td>
<td>7.1 mo (5.1, 12.6)</td>
</tr>
</tbody>
</table>
Atezolizumab 1a: ORR and OS Correlates with Level of TILs

Schmid et al, AACR 2017
No association of TMB, BRCA1/2, and LOH and Atezolizumab Activity

TMB (≥ 5.26 Mut/Mb), BRCA status or LOH at 14% are not associated to either response or overall survival.

Molinero et al, SABCS 2017
KEYNOTE 086 of Pembrolizumab: ORR by sTIL

Cohort B

<table>
<thead>
<tr>
<th>sTIL level</th>
<th>n</th>
<th>Responders</th>
<th>Ongoing responses</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥17.5%</td>
<td>23</td>
<td>9</td>
<td>5</td>
</tr>
<tr>
<td>&lt;17.5%</td>
<td>23</td>
<td>2</td>
<td>2</td>
</tr>
</tbody>
</table>

Cohort A

<table>
<thead>
<tr>
<th>sTIL level</th>
<th>n</th>
<th>Responders</th>
<th>Ongoing responses</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥5%</td>
<td>94</td>
<td>6</td>
<td>3</td>
</tr>
<tr>
<td>&lt;5%</td>
<td>53</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>

Combined Cohorts

<table>
<thead>
<tr>
<th>sTIL level</th>
<th>n</th>
<th>Responders</th>
<th>Ongoing responses</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥5%</td>
<td>135</td>
<td>17</td>
<td>10</td>
</tr>
<tr>
<td>&lt;5%</td>
<td>58</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>

Loi et al, ESMO 2017.
A phase 1b study of abemaciclib plus pembrolizumab for patients with HR+/HER2- MBC

- Abemaciclib induces synergistic immune activation and anti-tumor efficacy in combination with PD-L1 blockade

Eligibility: no prior CDKi, 1-2 prior chemo regimens; measurable disease, no h/o brain mets

Rugo et al, SABCS 2017
Disease Control Rate (CR + PR + SD) = 75.0%

Progressive disease (n = 5)
Stable disease (n = 17)
Partial response (n = 4)
Not assessed (n = 2)

Investigator Assessed Response N=28

Confirmed Objective Response Rate (ORR = CR + PR) (95% CI)

CR 0%
PR (confirmed) 14.3%

Monarch 1: 200 mg BID abemaciclib
• ORR: 6.8% at 16 weeks; 19.7% at final analysis
• Median time to response 3.7 months

Tumor size: % change from baseline

Rugo et al, SABCS 2017
An open-label, multitumor, Phase II basket study of olaparib and durvalumab (MEDIOLA): Results in germline BRCA-mutated (gBRCAm) HER2-negative MBC

Rationale: DNA damage has the potential to modify tumor immunogenicity; PARP inhibition upregulates PD-L1 expression

34 pts enrolled, 25 pts included here

36% first-line; 8% 3+ lines
36% prior platinum
48% HR+/52% TN
44% BRCA1; 56% BRCA2

Domcheck et al, SABCS 2017
- 12/25 (48%) had disease control at 28 weeks
- Unconfirmed ORR 52% (13/25) (60% in Olympiad)
- Median DOR/PFS/OS not yet reached

Domcheck et al, SABCS 2017
Study Design: PANACEA
IBCSG 45-13/BIG 4-13/KEYNOTE-014

Patients
- Centrally confirmed HER2+
- ECOG 0-1
- Tumor biopsy sample <1yr
- Measurable disease
- RECIST 1.1
- No limit of prior systemic treatment
- Documented PD on trastuzumab or TDM-1

PD-L1 +
- Phase Ib
  - Pembrolizumab 2mg/kg and 10mg/kg IV + trastuzumab Q3W

PD-L1 -
- Phase II
  - Pembrolizumab 200mg IV + trastuzumab Q3W

Protocol specified follow-up.
- Treatment until progression, toxicity, patient withdrawal, investigator decision, or maximum 2 years

Loi et al, SABCS 2017
In JAVELIN trial ORR to avelumab monotherapy in HER2+ cohort was 3.8% (n=26; unselected for PD-L1 status)

Loi et al, SABCS 2017; Dirix et al, BCRT 2017
Higher sTILs Associated with Better Response and Disease Control: PD-L1 Positive Cohorts

**Baseline sTILs and ORR**

- **Non-responders**
  - Baseline Stromal TILs: 0-10
- **Responders**
  - Baseline Stromal TILs: 10-40
- **P = 0.006**

**Baseline sTILs and DCR**

- **PD**
  - Baseline Stromal TILs: 0-10
- **CR, PR, SD ≥ 6 mos**
  - Baseline Stromal TILs: 10-40
- **P = 0.0006**

Loi et al, SABCS 2017
I-SPY 2 TRIAL Schema: HER2- Signatures

Adaptive Randomization

Paclitaxel

Paclitaxel + Pembro

Other HER2- Arms

12 weeks

Doxorubicin
60 mg/m2
Cyclophosphamide
600 mg/m2
X 4

8-12 weeks

SURGERY

Control
Paclitaxel 80 mg/m2 every wk x 12

Experimental
Paclitaxel 80 mg/m2 every wk x 12
Pembro 200 mg every 3 wks x 4

Nanda et al, ASCO 2017
### Pembrolizumab graduated in all HER2- signatures: Both HR+/HER2- and TN

<table>
<thead>
<tr>
<th>Signature</th>
<th>Estimated pCR rate (95% probability interval)</th>
<th>Probability pembro is superior to control</th>
<th>Predictive probability of success in phase 3</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pembro Control</td>
<td></td>
<td></td>
</tr>
<tr>
<td>All HER2-</td>
<td>0.46 (0.34 – 0.58) 0.16 (0.06 – 0.27)</td>
<td>&gt; 99%</td>
<td>99%</td>
</tr>
<tr>
<td>TNBC</td>
<td>0.60 (0.43 – 0.78) 0.20 (0.06 – 0.33)</td>
<td>&gt;99%</td>
<td>&gt;99%</td>
</tr>
<tr>
<td>HR+/HER2-</td>
<td>0.34 (0.19 – 0.48) 0.13 (0.03 – 0.24)</td>
<td>&gt;99%</td>
<td>88%</td>
</tr>
</tbody>
</table>
### Select treatment-related adverse events

<table>
<thead>
<tr>
<th></th>
<th>Pembrolizumab (n=69)</th>
<th>Control (n=180)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>% (n)</td>
<td>% (n)</td>
</tr>
<tr>
<td>All grades</td>
<td>Grades 3-5</td>
<td>All grades</td>
</tr>
<tr>
<td>Febrile neutropenia</td>
<td>7.2 (5)</td>
<td>6.7 (12)</td>
</tr>
<tr>
<td>Neutropenia w/o fever</td>
<td>5.8 (4)</td>
<td>1.7 (3)</td>
</tr>
<tr>
<td>Anemia</td>
<td>27.5 (19)</td>
<td>18.9 (34)</td>
</tr>
<tr>
<td>Fatigue</td>
<td>79.7 (55)</td>
<td>81.1 (146)</td>
</tr>
<tr>
<td>Nausea</td>
<td>73.9 (51)</td>
<td>71.7 (129)</td>
</tr>
<tr>
<td>Vomiting</td>
<td>34.8 (24)</td>
<td>18.3 (33)</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>49.3 (34)</td>
<td>37.8 (68)</td>
</tr>
<tr>
<td>Peripheral motor neuropathy</td>
<td>13.0 (9)</td>
<td>4.4 (8)</td>
</tr>
<tr>
<td>Peripheral sensory neuropathy</td>
<td>50.7 (35)</td>
<td>59.4 (107)</td>
</tr>
</tbody>
</table>

From start of treatment to 30 days after surgery (3 months after last dose of pembrolizumab)
Up to 60 days after treatment for those not undergoing surgery

Nanda et al, ASCO 2017
• Adrenal insufficiency reported in 6 patients
  • 5 presented after completion of AC (10-12 weeks after last pembro dose)
  • 1 presented during pembro treatment (5 weeks after 1st pembro dose)
• Primary and secondary AI are known toxicities of pembrolizumab
  • Rates across all studies are 0.8% and 0.6%

Nanda et al, ASCO 2017

<table>
<thead>
<tr>
<th></th>
<th>Pembrolizumab (n=69)</th>
<th>Control (n=180)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>% (n)</td>
<td>% (n)</td>
</tr>
<tr>
<td>All grades</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypothyroidism</td>
<td>8.7 (6)</td>
<td>0.6 (1)</td>
</tr>
<tr>
<td>Hyperthyroidism</td>
<td>4.3 (3)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Adrenal Insufficiency^</td>
<td>8.7 (6)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Hepatitis</td>
<td>2.9 (2)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Pneumonitis</td>
<td>2.9 (2)</td>
<td>1.1 (2)</td>
</tr>
<tr>
<td>Colitis</td>
<td>1.4 (1)</td>
<td>0.6 (1)</td>
</tr>
<tr>
<td>Pruritis</td>
<td>24.6 (17)</td>
<td>11.1 (20)</td>
</tr>
<tr>
<td>Grade 3-5</td>
<td>1.4 (1)</td>
<td>0 (0)</td>
</tr>
</tbody>
</table>
1. Monoclonal antibody specific for a tumor antigen with little/no expression on normal cells

2. Linker that is stable in circulation but releases the cytotoxic agent in target cells

3. Potent cytotoxic agent designed to induce target cell death when internalized and released
IMMU-132

- **Target:** Trop2 (EGP-1)
  - Pan-epithelial cancer antigen
  - Related to but distinct from EpCAM (EGP-2) – less expression on normal tissues.
  - Oncogene which signaling leading to increased tumorigenicity, aggressiveness, and metastasis.
  - Prognostic marker in several cancer types

- **Linker:** pH sensitive linker (CL2A)

- **Cytotoxic:** SN-38 (Irinotecan active metabolite)
Efficacy and Safety of Anti-Trop-2 Antibody Drug Conjugate Sacituzumab Govitecan (IMMU-132) in Heavily Pretreated Patients With Metastatic Triple-Negative Breast Cancer


Table 3. Treatment Efficacy in Intention-to-Treat Data Set (N = 69)

<table>
<thead>
<tr>
<th>Efficacy</th>
<th>Best Overall Response, No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CR</td>
<td>2 (3)</td>
</tr>
<tr>
<td>PR</td>
<td>19 (28)</td>
</tr>
<tr>
<td>SD</td>
<td>31 (45)</td>
</tr>
<tr>
<td>PD</td>
<td>17 (25)</td>
</tr>
<tr>
<td>Confirmed objective response (CR + PR)</td>
<td>21 (30)</td>
</tr>
<tr>
<td>95% CI</td>
<td>20 to 43</td>
</tr>
<tr>
<td>Clinical benefit (CR + PR + SD ≥ 6 months)</td>
<td>32 (46)</td>
</tr>
<tr>
<td>95% CI</td>
<td>34 to 59</td>
</tr>
<tr>
<td>Median duration of objective response, months (95% CI)</td>
<td>8.9 (6.1 to 11.3)</td>
</tr>
<tr>
<td>Median PFS, months (95% CI)</td>
<td>6.0 (5.0 to 7.3)</td>
</tr>
<tr>
<td>Median OS, months (95% CI)</td>
<td>16.6 (11.1 to 20.6)</td>
</tr>
</tbody>
</table>

N = 69. 66 patients with postbaseline target lesion measurements

J Clin Oncol 35:2141-2148.
### Select trials of Antibody-Drug Conjugates in Metastatic TNBC

<table>
<thead>
<tr>
<th>Name</th>
<th>Phase</th>
<th>Arms</th>
<th>Clinicaltrials.gov</th>
</tr>
</thead>
<tbody>
<tr>
<td>IMMU-132</td>
<td>III</td>
<td>Sacituzumab govitecan Capecitabine, eribulin, gemcitabine, vinorelbine</td>
<td>NCT02574455</td>
</tr>
<tr>
<td>CDX-011</td>
<td>II</td>
<td>Glembatumumab Capecitabine</td>
<td>NCT01997333</td>
</tr>
<tr>
<td>LIV1A</td>
<td>I/II</td>
<td>SGN-LIV1A</td>
<td>NCT01969643</td>
</tr>
</tbody>
</table>
A randomized, placebo-controlled, double-blind, phase II trial of nab-paclitaxel with or without mifepristone for advanced triple-negative breast cancer

**Key Eligibility**
- Metastatic TNBC
- GR+ by IHC (CLIA lab)
- 0-2 prior treatments
- PS 0-1
- Normal organ function
- Peripheral neuro < gr 2
- No prior nab-pac or mif

**Schema**
- Phase II
  - Nab-paclitaxel + Placebo
  - Nab-paclitaxel + Mifepristone

**Funded by Susan G. Komen Foundation**
Concept in Development: Randomized Phase II Pembrolizumab + Mifepristone for HER2- MBC

Hypothesis:
- Endogenous cortisol dampens immune checkpoint inhibition by suppressing cytotoxic Th1 cytokine response
- GR antagonism with Mif will shift the Th1/Th2 balance back to Th1 cytotoxic immune response, enhancing response to immune checkpoint inhibition

Cycle 1
- C1D1
- C1D8
- C1D15

Cycle 2
- C2D1
- C2D8
- C2D15

Cycle 3
- Pembro
- Mif
- Pembro
- Mif

= Biopsy
= Imaging
Thank You!

rnanda@medicine.bsd.uchicago.edu