Was gibt es neues beim metastasierten Mammakarzinom

Marcus Schmidt
Abteilung für Molekulare Onkologie
Klinik für Geburtshilfe und Frauengesundheit
Universitäres Centrum für Tumorerkrankungen
Universitätsmedizin Mainz

Conflict of Interest (COI)

- Forschungsunterstützung:
  - AstraZeneca, BioNTech, Eisai, German Breast Group, Genentech, Novartis, Palleos, Pantarhei Bioscience, Pfizer, Pierre-Fabre, Roche

- Vortragsstätigkeit:
  - AstraZeneca, Celgene, Eisai, Novartis, Pfizer, Pierre-Fabre, Roche

- Beratertätigkeit:
  - AstraZeneca, Celgene, Eisai, Lilly, Novartis, Pantarhei Bioscience, Pfizer, Pierre-Fabre, Roche, SeaGen
Correlative biomarker analysis of intrinsic subtypes and efficacy across the MONALEESA Phase III studies

Aleix Prat,1,3 Anwesha Chaudhury,4 Nadia Solovieff,4 Laia Parè,2,3 Debora Martinez,3 Nuria Chic,3 Olga Martinez-Sáez,1,3 Fara Brasó-Maristany,1,3 Karen Rodriguez-Lorencó,5 Teliana Taran,6 Naveen Babbar,6 Faye Su6

1Department of Medical Oncology, Hospital Clinic, Barcelona, Spain; 2SOLTI Breast Cancer Research Group, Barcelona, Spain; 3Translational Genomics and Targeted Therapies in Solid Tumors, Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), Barcelona, Spain; 4Novartis Institutes for BioMedical Research, Cambridge, MA; 5Novartis Pharmaceuticals Corporation, East Hanover, NJ; 6Novartis Pharma AG, Basel, Switzerland

This presentation is the intellectual property of the author/presenter. Contact them at ALEFRA@clinic.cat for permission to reprint and/or distribute.

San Antonio Breast Cancer Symposium®, December 9-12, 2020
**Intrinsic subtype distribution across the MONALEESA trials**

- The distribution of subtypes within each trial showed statistically significant differences, but when comparing the studies, the distribution of each subtype was similar, with luminal A being the most prevalent subtype and basal like being the least.

**Prognosis based on intrinsic subtype**

- Basal-like subtype had the worst prognosis in both treatment arms
- Intrinsic subtype was significantly associated with PFS in both the PBO (P < .0001) and RIB (P < .0001) arms
PFS analysis by subtype

- A PFS benefit of RIB vs PBO was observed in all subtypes except for basal like
- The interaction test between subtype and treatment arm was statistically significant ($P = .045$)

Conclusions

- This is the largest analysis evaluating the correlation of intrinsic subtype with efficacy outcomes in patients treated with CDK4/6 inhibitors
- These results confirm the independent prognostic value of the intrinsic subtypes in patients treated with ET alone
- The prognostic value of intrinsic subtype is maintained in the context of ET in combination with RIB

- Patients with HER2E, luminal A, and luminal B subtypes all exhibited a consistent PFS benefit with RIB treatment, while patients with basal-like subtype did not
- The HER2E subtype exhibited the greatest relative reduction in risk of progression or death with RIB plus ET
- Further validation studies will be required to firmly establish the clinical utility of intrinsic subtype as a biomarker in HR+/HER2− ABC
Methods (1 of 3)

Figure 1. Study Design of BYLieve (NCT03056755), a Phase II, Multicenter, Open-Label, 3-Cohort Noncomparative Study

**Men or postmenopausal women with HR+, HER2- ABC with a PIK3CA mutation**
- PIK3CA-mutated tumor tissue or blood
- Last line of therapy
- Eligible
- At least 21 days following the last cytotoxic chemotherapy or ET
- ECOG PS ≤ 2
- Measurable disease (per RECIST and/or ACR guidelines)
- No prior endocrine therapy
- Bone lesion

**Patients with CDK4/6i + AI as immediate prior treatment**

- Treatment: continuous until disease progression or unacceptable toxicity
- Dose interruptions and/or reductions allowed to enable continuing treatment

- Patients with progression of disease and received continuation of ET as immediate prior treatment

- Treatment crossover between cohorts is not permitted

**Primary endpoints**
- Proportion of patients alive without PD at 12 months (RECIST in each cohort)
- Secondary endpoints include:
  - PFS
  - DFS
  - OS
  - Safety

**Men in the letrozole cohort and postmenopausal women were allowed goserelin 3.6 mg SC every 28 days or leuprolide 7.5 mg IM every 28 days for adequate gonadal suppression.**

**Patients were enrolled and could stay on study based on confirmed PIK3CA mutation status from either tissue or blood by a certified local laboratory. Only patients with centrally confirmed PIK3CA mutation by a Novartis-designated laboratory were included in the mFAS.**

**Enrollment planned to be continued in each cohort until at least 112 patients with a centrally confirmed PIK3CA mutation were enrolled (102 total patients).**

**ET on D1 and D15 of Cycle 1 and D1 for all other cycles thereafter.**

**Oral QD.**

**Patients may receive ET as monotherapy or in combination with targeted treatment, except CDK4/6i + AI as immediate prior treatment. ET includes letrozole, fulvestrant and CDK4/6i plus letrozole.**

ABC, advanced breast cancer; AI, aromatase inhibitor; CB, common brittle; CDK4/6i, cyclin-dependent kinase 4 or 6 inhibitor; CTCAE, Common Terminology Criteria for Adverse Events; ECOG PS, Eastern Cooperative Oncology Group performance status; ET, endocrine therapy; HER2, human epidermal growth factor receptor 2; HR+, hormone receptor-positive; IV, intravenously; mFAS, modified full analysis set; OR, overall response; OS, overall survival; PFS, progression-free survival; PD, progressive disease; PIK3CA, phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha; QD, once daily; RECIST, Response Evaluation Criteria in Solid Tumors; SC, subcutaneously; SD, stable disease; SDH, succinate dehydrogenase; TTE, time to event; TVB, time to progression; Z4, less than 90 cm; Z5, greater than or equal to 90 cm.
Rugo et al., Alpelisib + Letrozole in Patients With PIK3CA-Mutated, Hormone Receptor-Positive (HR+), Human Epidermal Growth Factor Receptor 2-Negative (HER2–) Advanced Breast Cancer (ABC) Previously Treated With a Cyclin Dependent Kinase 4/6 Inhibitor (CDK4/6i) + Fulvestrant: BYLieve Study Results, SABCS 2020, Poster PD2-07

Results (6 of 13)
Figure 3. Kaplan–Meier Plot of Time to PFS per Local Investigator Assessment

- mPFS was 5.7 months (95% CI, 4.5-7.2 months; Figure 3)

CI, confidence interval; mPFS, median progression-free survival; No, number; PFS, progression-free survival.

Results (8 of 13)
Figure 4. Best Percentage Change From Baseline in Sum of Diameters per Investigator Assessment for Patients With Measurable Disease at Baseline in Cohorts A and B

- Cohort B (prior CDK4/6i + fulvestrant) showed a comparable reduction in tumor size to that observed in Cohort A (prior CDK4/6i + AI; Figure 4)

*Patients with missing best percentage change or those with best percentage change in target lesion but overall response of Unknown are excluded. Percentage change in target lesion contradicted by overall lesion response = PD.

AI, aromatase inhibitor; CDK4/6i, cyclin-dependent kinase 4 or 6 inhibitor.
Results (11 of 13)

Table 5. Safety of Alpelisib + Letrozole in the Prior CDK4/6i + Fulvestrant Cohort (Cohort B) (2 of 2)

<table>
<thead>
<tr>
<th>AEs by preferred term (≥20% all grades)</th>
<th>All Grades, n (%)</th>
<th>Grade ≥3, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diarrhea</td>
<td>85 (67.5)</td>
<td>5 (4.0)</td>
</tr>
<tr>
<td>Hyperglycemia</td>
<td>80 (63.5)</td>
<td>32 (25.4)</td>
</tr>
<tr>
<td>Nausea</td>
<td>69 (54.8)</td>
<td>3 (2.4)</td>
</tr>
<tr>
<td>Rash</td>
<td>39 (31.0)</td>
<td>12 (9.5)</td>
</tr>
<tr>
<td>Rash maculopapular&lt;sup&gt;c&lt;/sup&gt;</td>
<td>21 (16.7)</td>
<td>10 (7.9)</td>
</tr>
<tr>
<td>Fatigue</td>
<td>39 (31.0)</td>
<td>5 (4.0)</td>
</tr>
<tr>
<td>Decreased appetite</td>
<td>56 (44.4)</td>
<td>1 (0.8)</td>
</tr>
<tr>
<td>Stomatitis</td>
<td>43 (34.1)</td>
<td>1 (0.8)</td>
</tr>
<tr>
<td>Vomiting</td>
<td>31 (24.6)</td>
<td>1 (0.8)</td>
</tr>
<tr>
<td>Asthenia</td>
<td>27 (21.4)</td>
<td>5 (4.0)</td>
</tr>
</tbody>
</table>

A patient with multiple severity grades for an AE is only counted under the maximum grade. <sup>c</sup>Rash and rash maculopapular were recorded as separate preferred terms.

AE, adverse event; CDK4/6i, cyclin-dependent kinase 4 or 6 inhibitor.

Conclusions (1 of 2)

- Cohort B of BYLieve included patients who received any CDK4/6i + fulvestrant as immediate prior treatment for HR+, HER2−, PIK3CA-mutated ABC
  - Treatment included alpelisib + letrozole
  - Most (82%) had progressed on a prior AI
  - The primary endpoint was met: 46.1% (95% CI, 36.8%-55.6%) of patients were alive and without disease progression at 6 months
  - mPFS was 5.7 months (95% CI, 4.5-7.2 months)
  - Consistent with the well-characterized, manageable, and predictable safety profile for alpelisib, no new safety signals were observed
  - No difference in rash was observed in patients who received prophylactic antihistamines compared with patients who did not receive prophylactic antihistamines. This is in contrast to SOLAR-1<sup>6</sup> and BYLieve Cohort A<sup>5</sup>, in which prophylactic antihistamines decreased incidence and severity of rash, though small patient numbers make risk assessment difficult

ABC, advanced breast cancer; AI, aromatase inhibitor; CDK4/6i, cyclin-dependent kinase 4 or 6 inhibitor; CI, confidence interval; HER2−, human epidermal growth factor receptor 2−negative; HR+, hormone receptor-positive; mPFS, median progression-free survival; PIK3CA, phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha.
IMPACT OF TUCATINIB ON HEALTH-RELATED QUALITY OF LIFE IN PATIENTS WITH HER2+ METASTATIC BREAST CANCER WITH BRAIN METASTASES

Andrew Wardley1, Volkmar Mueller2, Elisavet Paplomata3, Laurence Crouzet4, Nayyer Iqbal5, Sramila Aithal6, Margaret Block7, Soren Cold8, Marie-Agnes By9, Olwen Hahn10, Teja Poosarla11, Erica Stringer-Reasor12, Marco Colleoni13, David Cameron14, Giuseppe Curigliano15, Kendra DeBusk16, Muriel Siadak16, Jorge Ramos16, Wentao Feng16, Karen Gelmon17

1Manchester Breast Centre, Division of Cancer Sciences, School of Medical Sciences, Faculty of Biology Medicine & Health, University of Manchester, Manchester, England; 2Department of Gynecology, University Medical Center Hamburg-Eppendorf, Hamburg, Germany; 3Carbone Comprehensive Cancer Center, University of Wisconsin-Madison, Madison, WI, USA; 4Center Eugene Marquis, Rennes, France; 5Saskatoon Cancer Centre, Saskatoon, Saskatchewan, Canada; 6Cancer Treatment Centers of America / Eastern Regional Medical Center, Philadelphia, PA, USA; 7Nebraska Cancer Specialist, Omaha, NE, USA; 8Odense University Hospital, Odense, Denmark; 9CHU Tours – Hospital Brestonnaux, Tours, France; 10University of Chicago Medical Center, Chicago, IL, USA; 11Mitchell Cancer Institute, University of South Alabama, Mobile, AL, USA; 12Division of Hematology and Oncology, University of Alabama at Birmingham, Birmingham, AL, USA; 13European Institute of Oncology, Milan, Italy; 14Edinburgh Cancer Research Centre, IGMM, University of Edinburgh, Edinburgh, Scotland; 15European Institute of Oncology, IRCCS, and University of Milano, Milan, Italy; 16Seagen Inc., Bothell, WA, USA; 17British Columbia Cancer Agency–Vancouver Centre, Vancouver, BC, Canada

San Antonio Breast Cancer Symposium®; December 8–11, 2020; Poster No. PD13-04

FOR REACTIVE SCIENTIFIC EXCHANGE; NOT FOR DISTRIBUTION OR PROMOTIONAL USE
Study Design

Key Eligibility Criteria

- HER2+ MBC
- Prior treatment with trastuzumab, pertuzumab, and T-DM1
- ECOG performance status 0 or 1
- Brain MRI at baseline

Tucatinib 300 mg PO BID
Trastuzumab 6 mg/kg Q3W, loading dose 8 mg/kg C1D1
Capecitabine 1000 mg/m² PO BID Days 1–14

Placebo
Trastuzumab 6 mg/kg Q3W, loading dose 8 mg/kg C1D1
Capecitabine 1000 mg/m² PO BID Days 1–14

HRQoL with Brain Metastases Study Population

- Assessments initiated in August 2017
- HRQoL data were available from 331 of 612 patients, including 164 patients with brain metastases:
  - 107 patients in the tucatinib arm
  - 57 patients in the placebo arm

HRQoL Assessments

- Overall health status: visual analog scale (VAS)
- Time to deterioration of QoL: defined as decrease of 7 points on VAS
- Change from baseline on individual patient-reported items
  - Mobility, self-care, usual activities, pain/discomfort, and anxiety/depression
  - Each dimension has 5 levels: no, slight, moderate, severe, or extreme problems
• HRQoL was maintained throughout treatment and was not noticeably different between treatment arms.

- Addition of tucatinib significantly delayed time to worsening of EQ-5D-5L Health Score.
  - Compared to the placebo arm, patients on the tucatinib arm had a 49% reduction in the risk of deterioration

<table>
<thead>
<tr>
<th></th>
<th>Events/Total</th>
<th>HR (95% CI)</th>
<th>Median (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TUC+Tras+Cape</td>
<td>26/107</td>
<td>0.51 (0.28, 0.93)</td>
<td>5.5 months (4.2, --)</td>
</tr>
<tr>
<td>Pbo+Tras+Cape</td>
<td>20/56</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Time to Worsening (≥7 points) in EQ-5D-5L Health Score in HRQoL Population with Brain Metastases
Conclusions

- In HER2+ MBC patients with brain metastases, tucatinib in combination with trastuzumab and capecitabine demonstrates significantly longer and clinically meaningful time to deterioration of HRQoL.

- Patients, including those with brain metastases, treated with tucatinib, trastuzumab, and capecitabine maintain HRQoL throughout the treatment period, which was longer compared to patients treated with only trastuzumab and capecitabine.10

- These results, together with the HER2CLIMB primary analysis and the HRQoL analysis in the total population, demonstrate that this regimen improves PFS and OS, and maintains QoL in all patients, including those with brain metastases.
Baseline Patient Characteristics

- Baseline demographics and disease characteristics in HR+/HR- subgroups were generally balanced between treatment arms.

<table>
<thead>
<tr>
<th></th>
<th>HR+</th>
<th>HR-</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>TUC+Tras+Cape (N=243)</td>
<td>Pbo+Tras+Cape (N=127)</td>
</tr>
<tr>
<td>Age in years, median (range)</td>
<td>55.0 (22, 80)</td>
<td>54.0 (31, 82)</td>
</tr>
<tr>
<td>Female, n (%)</td>
<td>240 (98.8)</td>
<td>125 (98.4)</td>
</tr>
<tr>
<td>ECOG performance status, n (%)</td>
<td>121 (49.8)</td>
<td>64 (50.4)</td>
</tr>
<tr>
<td>Stage IV at initial diagnosis, n (%)</td>
<td>122 (50.2)</td>
<td>63 (49.6)</td>
</tr>
<tr>
<td>Prior lines of therapy, median (range)</td>
<td>Overall</td>
<td>4.0 (2.14)</td>
</tr>
<tr>
<td>Presence/history of brain metastases, n (%)</td>
<td>Metastatic setting</td>
<td>3.0 (1, 14)</td>
</tr>
</tbody>
</table>

PFS by HR Status in the Primary Endpoint Population

- PFS benefit was observed in patients in the tucatinib arm of the primary endpoint population regardless of hormone receptor status.

PFS by BICR in HR+ Subgroup

PFS by BICR in HR- Subgroup
Clinically meaningful improvement of OS was observed in patients on the tucatinib arm regardless of hormone receptor status.

Of the HR+ patients who discontinued or never received tucatinib or placebo, 16% (n=23/172) in the tucatinib arm and 15% (n=16/108) in the placebo arm received one or more subsequent new hormonal therapies.

OS benefit favoring the tucatinib arm was observed in patients with brain metastases regardless of hormone receptor status.

PFS benefit favoring the tucatinib arm was observed in patients with brain metastases regardless of hormone receptor status.
OS by HR Status in Patients with Baseline Brain Metastases

- OS was numerically improved in patients with brain metastases in the tucatinib arm in both hormone receptor subgroups.

Conclusions

- Tucatinib is the first tyrosine kinase inhibitor to demonstrate prolonged OS in patients with and without brain metastases with HER2+ MBC in a randomized, controlled trial.\(^2\)
  - HER2CLIMB was not powered to detect a difference in outcomes by hormone receptor status; however, the hazard ratios for both HR+ and HR- subgroups reveal a consistent benefit in OS for patients treated with tucatinib, trastuzumab, and capecitabine.

- Tucatinib in combination with trastuzumab and capecitabine demonstrate clinically meaningful improvements in PFS regardless of hormone receptor status in patients with HER2+ MBC, with and without brain metastases.

- The observed benefit of tucatinib regardless of hormone receptor status was consistent with the overall outcome in the HER2CLIMB primary analysis and demonstrate that tucatinib in combination with trastuzumab and capecitabine is an active regimen in patients with HER2+ MBC.
Biomarker Evaluation in the Phase 3 ASCENT Study ofSacituzumab Govitecan Versus Chemotherapy in Patients With Metastatic Triple-Negative Breast Cancer

Sara A. Hurvitz,1 Sara M. Tolane,2 Kevin Punie,3 Delphine Loirat,4 Mafalda Oliveira,5 Kevin Kalinsky,6 Amelia Zelnak,7 Philippe Aflimos,8 Florence Dalenc,9 Sagar Sardesai,10 Erika Hamilton,11 Priyanka Sharma,12 Sabela Recalde,13 Eva Ciruelos Gil,14 Tiffany Traina,15 Joyce O'Shaughnessy,16 Javier Cortes,17 Michaela Tsai,18 Linda Vahdat,19 Véronique Diéras,20 Lisa Carey,21 Hope S. Rugo,22 David M. Goldenberg,23 Quan Hong,23 Martin Olivo,23 Loretta M. Iri,23 and Aditya Bardia24

1Medical Oncology, University of California, Los Angeles, Jonsson Comprehensive Cancer Center, Los Angeles, CA, USA; 2Dana-Farber Cancer Institute, Boston, MA, USA; 3Department of General Medical Oncology, University Hospitals Leuven, Leuven, Belgium; 4Institut Lurc, Paris, France; 5Hospital Universitari Vall d'Iberson, Barcelona, Spain; 6Winship Cancer Institute, Emory University, Atlanta, GA, USA; 7Northwest Hospital, Atlanta, GA, USA; 8Institut Jules Bordet, Brussels, Belgium; 9Institut Claudius Regaud, Toulouse, France; 10The Ohio State University Wexner Medical Center, Columbus, OH, USA; 11Sarah Cannon Research Institute/Tennessee Oncology, Nashville, TN, USA; 12University of Kansas Cancer Center - The Richard and Annette Bloch Cancer Care Pavilion, Kansas City, KS, USA; 13Institut Catala d'Oncoologia Hospitalat, Barcelona, Spain; 14Hospital Universitari 12 de Octubre, Madrid, Spain; 15Memorial Sloan Kettering Cancer Center, New York, NY, USA; 16Texas Oncology - Baylor Charles A. Sammons Cancer Center, Dallas, TX, USA; 17KIR Institute of Oncology, Girona Group, Madrid & Barcelona, Spain; 18Parkway Oncology Research, Minneapolis, MN, USA; 19Memorial Sloan Kettering Cancer Center, New York, NY, USA; 20Centre Eugène-Mᵃʳⁿᵉⁿ, Rennes, France; 21University of North Carolina Lineberger Comprehensive Cancer Center, Chapel Hill, NC, USA; 22University of California San Francisco Comprehensive Cancer Center, San Francisco, CA, USA; 23Memorial Sloan Kettering Cancer Center, New York, NY, USA; 24Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA


ClinicalTrials.gov Number: NCT03554465
ASCENT: A Phase 3 Confirmatory Study of Sacituzumab Govitecan in Refractory/Relapsed mTNBC

**Metastatic TNBC**
(per ASCO/CAP)
≥2 chemotherapies for advanced disease
(no upper limit; 1 of the required prior regimens could be progression occurred within a 12-month period after completion of (neo)adjuvant therapy)
N=529

**Sacituzumab Govitecan (SG)**
10 mg/kg IV
days 1 & 8, every 21-day cycle
(n=287)

**Treatment of Physician’s Choice (TPC)**
(n=233)

**Endpoints**
Primary
• PFS
Secondary
• PFS for the full population
• OS, ORR, DOR, TTR, safety
Exploratory
• Biomarkers

**Stratification factors**
- Number of prior chemotherapies (2-3 vs >3)
- Geographic region (North America vs Europe)
- Presence/absence of known brain metastases (yes/no)

We report the exploratory biomarker analysis in the brain metastases-negative (Brain Mets-Negative) population

---

**Demographics (Brain Mets-Negative)**

<table>
<thead>
<tr>
<th></th>
<th>SG (n=233)</th>
<th>TPC (n=233)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Female—no. (%)</strong></td>
<td>233 (99)</td>
<td>233 (100)</td>
</tr>
<tr>
<td><strong>Median age—yr (range)</strong></td>
<td>54 (25-82)</td>
<td>53 (27-81)</td>
</tr>
<tr>
<td><strong>Race or ethnic group—no. (%)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>188 (80)</td>
<td>181 (78)</td>
</tr>
<tr>
<td>Black</td>
<td>26 (12)</td>
<td>26 (12)</td>
</tr>
<tr>
<td>Asian</td>
<td>9 (4)</td>
<td>9 (4)</td>
</tr>
<tr>
<td>Other or not specified</td>
<td>10 (4)</td>
<td>15 (6)</td>
</tr>
<tr>
<td><strong>ECOG PS—no. (%)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>108 (46)</td>
<td>98 (42)</td>
</tr>
<tr>
<td>1</td>
<td>127 (54)</td>
<td>135 (58)</td>
</tr>
<tr>
<td><strong>BRCA1/2 mutational status—no. (%)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive</td>
<td>16 (7)</td>
<td>18 (8)</td>
</tr>
<tr>
<td>Negative</td>
<td>133 (57)</td>
<td>125 (54)</td>
</tr>
<tr>
<td><strong>Trop-2 expression—no. (%)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(High) H-score 200-300</td>
<td>85 (36)</td>
<td>72 (52)</td>
</tr>
<tr>
<td>(Medium) H-score 100-200</td>
<td>39 (17)</td>
<td>35 (25)</td>
</tr>
<tr>
<td>(Low) H-score &lt;100</td>
<td>27 (12)</td>
<td>32 (23)</td>
</tr>
</tbody>
</table>

**Original diagnosis of TNBC**

<table>
<thead>
<tr>
<th></th>
<th>SG (n=233)</th>
<th>TPC (n=233)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Yes</strong></td>
<td>166 (70)</td>
<td>157 (67)</td>
</tr>
<tr>
<td><strong>No</strong></td>
<td>70 (30)</td>
<td>76 (33)</td>
</tr>
<tr>
<td><strong>Previous antineoplastic regimens—median (range)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Taxane</td>
<td>4 (2-17)</td>
<td>4 (2-14)</td>
</tr>
<tr>
<td>Cyclophosphamide</td>
<td>102 (62)</td>
<td>102 (62)</td>
</tr>
<tr>
<td>Carboplatin</td>
<td>147 (63)</td>
<td>160 (89)</td>
</tr>
<tr>
<td><strong>Capcitabine</strong></td>
<td>147 (63)</td>
<td>165 (88)</td>
</tr>
<tr>
<td><strong>Previous PARP inhibitor—no. (%)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lung only</td>
<td>108 (46)</td>
<td>97 (42)</td>
</tr>
<tr>
<td>Liver</td>
<td>98 (42)</td>
<td>101 (43)</td>
</tr>
<tr>
<td>Bone</td>
<td>48 (20)</td>
<td>50 (21)</td>
</tr>
</tbody>
</table>

Assessed in the brain metastases-negative population. *Patients in study either had TNBC at initial diagnosis or had hormone receptor-positive disease that converted to hormone-negative at time of study entry.*

*Antitumor regimens refer to any treatment regimen that was used to treat breast cancer in any setting. Includes palliative, palliatively based, and disease-based. *Based on independent central review of target and metastatic lesion at baseline.

BRCA, breast cancer gene; ECOG-PS, Eastern Cooperative Oncology Group performance status; IHC, immunohistochemical score; PARP, polyadenosine diphosphate ribose polymerase.

SG, sacituzumab govitecan; TPC, triple-negative breast cancer; TPC, treatment of physician’s choice; Trop-2, breast-specific antigen. 2

This presentation is the intellectual property of the author/presenter. Contact them at shrinidhiserpentax.a.ed for permission to reprint and/or distribute.
Progression-Free Survival by Trop-2 Expression

Assessed in brain-metastases negative population, Trop-2 expression determined in archival samples by validated immunohistochemistry assay and H-scoring.

Overall Survival by Trop-2 Expression

Assessed in brain-metastases negative population, Trop-2 expression determined in archival samples by validated immunohistochemistry assay and H-scoring.

This presentation is the intellectual property of the authors/presenter. Contact them at skurod@mgh.harvard.edu for permission to reprint and/or distribute.
**ORR by Trop-2 Expression**

<table>
<thead>
<tr>
<th>Trop-2 Expression</th>
<th>H-score</th>
<th>ORR (%)</th>
<th>(95% CI)</th>
<th>SG (n=85)</th>
<th>TPC (n=72)</th>
<th>SG (n=39)</th>
<th>TPC (n=35)</th>
<th>SG (n=27)</th>
<th>TPC (n=32)</th>
</tr>
</thead>
<tbody>
<tr>
<td>High (n=157)</td>
<td>200-300</td>
<td>44%</td>
<td>33-55</td>
<td>1% (1)</td>
<td>11% (4)</td>
<td>9-42</td>
<td>6% (2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medium (n=74)</td>
<td>100-200</td>
<td>38%</td>
<td>23-55</td>
<td>3-27</td>
<td>9-42</td>
<td>1-21</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low (n=59)</td>
<td>&lt;100</td>
<td>22%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Assessed in the breast metastases-negative population. ORR and PFS are assessed by BICR. Trop-2 expression determined in archival samples by validated immunohistochemistry assay and H-scoring. BICR, blind independent central review; H-score, histopathological score; ORR, objective response rate; SG, semisubcutaneous placebo; TPC, treatment of physician’s choice; Trop-2, trophoblast cell surface antigen-2.

**Conclusions**

- Outcomes in these subgroups confirm that clinical benefit with SG versus TPC in previously treated mTNBC is irrespective of level of Trop-2 expression
  - Higher efficacy outcomes were observed in patients treated with SG who had a medium/high Trop-2 H-score (vs low Trop-2 H-score) versus those treated with TPC
- SG outperformed TPC regardless of germline *BRCA1/2* mutation status at study entry
- Caution should be exercised in data interpretation given the small sample sizes in the Trop-2 low subgroup and germline *BRCA1/2*-positive subgroup
- Trop-2 expression did not affect toxicity, and SG demonstrates a manageable safety profile consistent with that of the ASCENT overall study population and shown in previous reports

BRCA, breast cancer gene; H-score, histopathological score; mTNBC, metastatic triple-negative breast cancer; SG, semisubcutaneous placebo; TPC, treatment of physician’s choice; Trop-2, trophoblast cell surface antigen-2.
Double-blind placebo-controlled randomized phase III trial evaluating first-line ipatasertib combined with paclitaxel for PIK3CA/AKT1/PTEN-altered locally advanced unresectable or metastatic triple-negative breast cancer: Primary results from IPATunity130 Cohort A

Rebecca A Dent, M.D., on behalf of


1National Cancer Centre Singapore, Singapore; 2Asan Medical Center, University of Ulsan College of Medicine, Seoul, South Korea; 3Vall d’Hebron University Hospital, Vall d’Hebron Institute of Oncology (VHIO), Barcelona, Spain; 4Latin American Cooperative Oncology Group, Porto Alegre RS, Brazil; 5Baylor University Medical Center, Texas Oncology, U.S. Oncology, Dallas, TX, USA; 6Massachusetts General Hospital, Boston, MA, USA; 7Fukushima Medical University Hospital, Fukushima City, Fukushima, Japan; 8Hospital Arauto Jorge, Goiania, Brazil; 9Unidad de Investigación, Instituto de Oncología y Radioterapia, Clínica Ricardo Palma, San Isidro, Peru; 10City Clinical Hospital No. 4, Dnipropetrovsk, Ukraine; 11Genentech, Inc., South San Francisco, CA, USA; 12Roche Products Ltd, Welwyn Garden City, UK; 13Hoffmann-La Roche Ltd, Basel, Switzerland; 14The Royal Marsden NHS Foundation Trust, London, UK and Breast Cancer Now Research Centre, The Institute of Cancer Research, London, UK

This presentation is the intellectual property of the presenter. Contact her at rebecca.dent@duke-nus.edu.sg for permission to reprint and/or distribute.

IPATunity130 Cohort A (NCT03337724): Double-blind placebo-controlled randomized trial

- Measurable aTNBC
- PIK3CA/AKT1/PTEN alterationa
- No prior chemotherapy for a TNBC ≥12 months since last (neo)adjuvant chemotherapy
- Candidate for taxane therapy
- ECOG performance status 0/1

Analysis of primary endpoint (investigator-assessed PFS) planned after 125 PFS events
- 95.5% power to detect an increase in median PFS of 6 → 12 months with addition of IPAT to PAC
- Target HR = 0.50 at 2-sided 5% significance level

255 patients enrolled between Feb 6, 2018, and Apr 8, 2020.

Stratification factors:
- Prior (neo)adjuvant chemotherapy (yes vs no)
- Geographic region (Asia-Pacific vs Europe vs North America vs rest of world)
- Tumor alteration status (PIK3CA/AKT1-activating mutation vs PTEN alteration without PIK3CA/AKT1-activating mutation)

Gastrointestinal toxicity or hematological toxicity

Treatment until disease progression, intolerable toxicity, or elective withdrawal

Crossover from PBO to IPAT is not permitted

R 2:1

PAC 80 mg/m2 days 1, 8 & 15 +
IPAT 400 mg qd days 1–21 q28d

PAC 80 mg/m2 days 1, 8, & 15
+ PBO days 1–21 q28d

28.01.2021
**Baseline characteristics**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>PRO + PAC (n=87)</th>
<th>IPAT + PAC (n=168)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age, years</strong></td>
<td>53 (25–80)</td>
<td>56 (27–81)</td>
</tr>
<tr>
<td><strong>Region</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asia Pacific</td>
<td>18 (21)</td>
<td>36 (21)</td>
</tr>
<tr>
<td>Europe</td>
<td>35 (40)</td>
<td>70 (42)</td>
</tr>
<tr>
<td>North America</td>
<td>4 (5)</td>
<td>4 (2)</td>
</tr>
<tr>
<td>Rest of world</td>
<td>30 (34)</td>
<td>58 (35)</td>
</tr>
<tr>
<td><strong>Prior (neo)adjuvant chemotherapy</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1–3</td>
<td>22 (25)</td>
<td>44 (26)</td>
</tr>
<tr>
<td>&gt;3</td>
<td>20 (23)</td>
<td>32 (19)</td>
</tr>
<tr>
<td>No prior chemotherapy</td>
<td>38 (45)</td>
<td>87 (52)</td>
</tr>
<tr>
<td>Not available</td>
<td>4 (5)</td>
<td>5 (3)</td>
</tr>
<tr>
<td><strong>Disease status</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Locally advanced unresectable</td>
<td>11 (13)</td>
<td>16 (21)</td>
</tr>
<tr>
<td>Metastatic</td>
<td>76 (87)</td>
<td>132 (70)</td>
</tr>
<tr>
<td><strong>Metastatic sites</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lung</td>
<td>30 (41)</td>
<td>60 (39)</td>
</tr>
<tr>
<td>Liver</td>
<td>23 (26)</td>
<td>37 (22)</td>
</tr>
<tr>
<td>Bone</td>
<td>29 (33)</td>
<td>56 (33)</td>
</tr>
<tr>
<td>Lymph node</td>
<td>55 (63)</td>
<td>93 (55)</td>
</tr>
<tr>
<td><strong>PD-L1 status</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive</td>
<td>35 (40)</td>
<td>48 (29)</td>
</tr>
<tr>
<td>Negative</td>
<td>28 (32)</td>
<td>65 (39)</td>
</tr>
<tr>
<td>Unknown</td>
<td>24 (28)</td>
<td>55 (33)</td>
</tr>
<tr>
<td><strong>FMI status</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PI3KCA/ AKT1 activating mutation</td>
<td>44 (51)</td>
<td>86 (51)</td>
</tr>
<tr>
<td>PTEN alteration without PI3KCA/AKT1-activating mutation</td>
<td>43 (49)</td>
<td>82 (49)</td>
</tr>
</tbody>
</table>

*1 year in 2 PBO + PAC patients. **Reported for only 70 PBO + PAC and 132 IPAT + PAC patients with metastatic (no locally advanced unresectable) disease at baseline. One additional PBO + PAC patient had metastatic disease but no sites recorded.

This presentation is the intellectual property of the presenter. Contact her at rebecca.dent@duke-nus.edu.sg for permission to reprint and/or distribute.

---

**Primary endpoint: Investigator-assessed PFS**

**Data cut-off: May 7, 2020 (median follow-up: 8.3 months)**

<table>
<thead>
<tr>
<th>PFS</th>
<th>PBO + PAC (n=87)</th>
<th>IPAT + PAC (n=168)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients with events, n (%)</td>
<td>40 (30)</td>
<td>92 (50)</td>
</tr>
<tr>
<td>Median PFS, months (95% CI)</td>
<td>6.1 (5.5–9.8)</td>
<td>7.4 (5.6–8.5)</td>
</tr>
<tr>
<td>Stratified PFS HR (95% CI)</td>
<td>1.02 (95% CI 0.71–1.45)</td>
<td></td>
</tr>
</tbody>
</table>

Log-rank p=0.0237

This presentation is the intellectual property of the presenter. Contact her at rebecca.dent@duke-nus.edu.sg for permission to reprint and/or distribute.
### Conclusions

- Adding the AKT inhibitor ipatatasertib to paclitaxel in patients with \(PIK3CA/AKT1/PTEN\)-altered aTNBC did not significantly improve PFS
  - Overall survival follow-up is ongoing
- Safety was consistent with previously reported results for this combination\(^1\)
- Results from this trial differ from findings in both randomised phase II trials of AKT inhibition in aTNBC: LOTUS (paclitaxel ± ipatasertib)\(^1\) and PAKT (paclitaxel ± capivasertib)\(^2\)
  - Further analyses of IPATunity130 Cohort A are ongoing to explore potential biomarkers of benefit from ipatasertib


This presentation is the intellectual property of the presenter. Contact her at rebecca.dent@duke-nus.edu.sg for permission to reprint and/or distribute.
Additional Efficacy Endpoints from the Phase 3 KEYNOTE-355 Study of Pembrolizumab + Chemotherapy versus Placebo + Chemotherapy as First-Line Therapy for Locally Recurrent Inoperable or Metastatic Triple-Negative Breast Cancer (mTNBC)

Hope S. Rugo1, Peter Schmid2, David W. Cescon2, Zbigniew Nowecki3, Seock-AN Im2, Mastura Md Yusop4, Carlos Gallardo5, Oleg Lipatov6, Carlos Henrique Barrios6, Jose Perez-Garcia7, Hiroji Iwata7, Norikazu Masuda8, Marco Torregroza Otero9, Erhan Golmen10, Sherene Loi11, Zifang Guo12, Jing Zhao12, Vassiliki Karantza12, Gursel Akten13, Javier Cortes17

1. University of California San Francisco Comprehensive Cancer Center, San Francisco, CA, USA; 2. Barts Cancer Institute, Centre for Experimental Cancer Medicine, Queen Mary University of London, London, UK; 3. Princess Margaret Cancer Centre, Toronto, Ontarto, Canada; 4. Maria Sklodowska-Curie Memorial Cancer Centre and Institute of Oncology, Warsaw, Poland; 5. Seoul National University Hospital, Seoul, Korea; 6. Pantai Hospital, Kuala Lumpur, Malaysia; 7. Arturo Lopez Perez Foundation, Santiago, Chile; 8. Republican Clinical Oncology Dispensary, Republic of Dagesthan, Russian Federation; 9. Centro de Oncología, Porto Alegre, Brazil; 10. Institute of Breast Cancer, Quiron Group, Barcelona; 11. Aichi Cancer Center Hospital, Nagoya, Japan; 12. National Hospital Organization Osaka National Hospital, Osaka, Japan; 13. Oncomedica S.A., Monteria, Colombia; 14. Ege University Medical Faculty, Izmir, Turkey; 15. Peter McCallum Cancer Institute, Melbourne, Australia; 16. Marvin & Co., Inc., Komelworth, N.J, U.S.A.; 17. International Breast Cancer Center (IBCC), Quiron Group, Madrid & Barcelona, Spain

This presentation is the intellectual property of Hope Rugo. Contact her at Hope.Rugo@ucsf.edu for permission to reprint and/or distribute.

KEYNOTE-355 Study Design (NCT02819857)

Key Eligibility Criteria:
- Age ≥18 years
- Central determination of TNBC and PD-L1 expression
- Previously untreated locally recurrent inoperable or metastatic TNBC
- Completion of treatment with curative intent 26 months prior to first disease recurrence
- ECOG performance status 0 or 1
- Life expectancy ≥12 weeks from randomization
- Adequate organ function
- No systemic steroids
- No active CNS metastasis
- No active autoimmune disease

Pembrolizumab + Chemotherapy

Progressive disease/cessation of study therapy

Placebo + Chemotherapy

Stratification Factors:
- Chemotherapy on study (taxane vs gemcitabine-carboplatin)
- PD-L1 tumor expression (CPS ≥1 vs CPS <1)
- Prior treatment with same class chemotherapy in the neoadjuvant or adjuvant setting (yes vs no)

*Pembrolizumab 200 mg IV Q3W.
*Chemotherapy dosing from here are as follows:
Nab-paclitaxel 100 mg/m² IV on days 1, 8, and 15 every 28 days.
Sorafenib 400 mg PO on days 1, 8, and 15 every 28 days.
Gemcitabine 1000 mg/m² carboplatin AUC 2 on days 1 and 8 every 21 days.

This presentation is the intellectual property of Hope Rugo. Contact her at Hope.Rugo@ucsf.edu for permission to reprint and/or distribute.
Baseline Characteristics, ITT

<table>
<thead>
<tr>
<th>Characteristic, n (%)</th>
<th>Pembrolizumab + Chemo N = 566</th>
<th>Placebo + Chemo N = 281</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, median (range), yrs</td>
<td>53 (25-85)</td>
<td>53 (22-77)</td>
</tr>
<tr>
<td>ECOG PS 1</td>
<td>232 (41.0)</td>
<td>108 (38.4)</td>
</tr>
<tr>
<td>PD-L1–positive CPS ≥1</td>
<td>425 (75.1)</td>
<td>711 (75.1)</td>
</tr>
<tr>
<td>PD-L1–positive CPS ≤10</td>
<td>220 (39.9)</td>
<td>103 (36.7)</td>
</tr>
<tr>
<td>Chemotherapy on study</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nab-Paclitaxel</td>
<td>173 (30.0)</td>
<td>95 (33.0)</td>
</tr>
<tr>
<td>Paclitaxel</td>
<td>82 (14.5)</td>
<td>32 (11.4)</td>
</tr>
<tr>
<td>Carmustine-Carboplatin</td>
<td>311 (54.0)</td>
<td>164 (54.0)</td>
</tr>
<tr>
<td>Prior same-class chemotherapy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>124 (21.9)</td>
<td>62 (22.1)</td>
</tr>
<tr>
<td>No</td>
<td>442 (78.1)</td>
<td>219 (77.9)</td>
</tr>
</tbody>
</table>

This presentation is the intellectual property of Hope Rugo. Contact her at Hope.Rugo@ucsf.edu for permission to reprint and/or distribute.

Progression-Free Survival: PD-L1 CPS ≥1

- **Pembrolizumab + Chemo**
  - 136/230 (59.1%)
  - HR (95% CI): 0.66 (0.49-0.88)
  - P-value (one-sided): 0.0012

- **Placebo + Chemo**
  - 79/103 (76.7%)

---

Hazard ratio (HR) analyzed based on a Cox regression model with treatment as a covariate stratified by the randomization stratification factors. Data cut-off December 11, 2019.

This presentation is the intellectual property of Hope Rugo. Contact her at Hope.Rugo@ucsf.edu for permission to reprint and/or distribute.
Progression-Free Survival: PD-L1 CPS ≥ 50

- Pembro + Chemo: 288/425, 67.8% 7.6 months (95% CI: 0.74, 0.9014)
- Placebo + Chemo: 162/211, 70.8% 5.6 months

Progression-Free Survival: ITT

- Pembro + Chemo: 901/566, 69.1% 7.3 months (95% CI: 0.83, 0.97)
- Placebo + Chemo: 211/281, 75.1% 5.9 months

Notes:
- Prespecified P-value boundary of 0.00111 not met.
- Hazard ratio (CI) analyzed based on a Cox regression model with treatment as a covariate stratified by the randomization stratification factors. Data cutoff December 11, 2019.
- This presentation is the intellectual property of Hope Rugo. Contact her at Hope.Rugo@ucsf.edu for permission to reprint and/or distribute.
Progression-Free Survival in Subgroups On-Study Chemotherapy

PD-L1 CPS ≥10  PD-L1 CPS ≥1  ITT

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>N</th>
<th>Median PFS (mo)</th>
<th>Hazard Ratio for Progression or Death (95% CI)</th>
<th>N</th>
<th>Median PFS (mo)</th>
<th>Hazard Ratio for Progression or Death (95% CI)</th>
<th>N</th>
<th>Median PFS (mo)</th>
<th>Hazard Ratio for Progression or Death (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>323</td>
<td>9.7</td>
<td>5.8 (0.46 to 0.86)</td>
<td>636</td>
<td>7.6</td>
<td>5.6 (0.81 to 0.92)</td>
<td>847</td>
<td>7.5</td>
<td>5.6 (0.89 to 0.92)</td>
</tr>
<tr>
<td>Un-study chemotherapy</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pembrolizumab</td>
<td>58</td>
<td>0.9</td>
<td>0.37 (0.54 to 0.59)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Placebo</td>
<td>54</td>
<td>3.4</td>
<td>0.22 (0.11 to 0.76)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall</td>
<td>112</td>
<td>0.9</td>
<td>0.67 (0.41 to 1.15)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pembrolizumab</td>
<td>60</td>
<td>7.8</td>
<td>0.77 (0.45 to 1.31)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Placebo</td>
<td>52</td>
<td>7.7</td>
<td>0.80 (0.46 to 1.39)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pembrolizumab + Chemo</td>
<td>45</td>
<td>7.4</td>
<td>0.74 (0.46 to 1.21)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Placebo + Chemo</td>
<td>52</td>
<td>7.4</td>
<td>0.83 (0.48 to 1.42)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The PFS treatment effect was assessed in subgroups descriptively using hazard ratios and 95% CIs; although subgroup analyses by on-study chemotherapy were pre-specified, the trial was not powered to compare efficacy among treatment groups by different chemotherapy regimens. Steroid premedication for radiolabeled was given according to local guidelines and practices and was not restricted by the protocol. Steroid use was also allowed for the management of immune-mediated AEs across the study. Data cutoff December 11, 2019.

This presentation is the intellectual property of Hope Rugo. Contact her at Hope.Rugo@ucsf.edu for permission to reprint and/or distribute.

Response Rate

PD-L1 CPS ≥10  PD-L1 CPS ≥1  ITT

<table>
<thead>
<tr>
<th>Group</th>
<th>N</th>
<th>ORR (%) (95% CI)</th>
<th>DCR (%) (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pembrolizumab + Chemo (N = 220)</td>
<td>53.2 (46.4–59.9)</td>
<td>65.0 (68.3–71.3)</td>
<td></td>
</tr>
<tr>
<td>Placebo + Chemo (N = 103)</td>
<td>39.9 (30.3–49.9)</td>
<td>54.4 (44.3–64.2)</td>
<td></td>
</tr>
<tr>
<td>Pembrolizumab + Chemo (N = 425)</td>
<td>45.2 (40.4–50.0)</td>
<td>58.6 (53.7–63.3)</td>
<td></td>
</tr>
<tr>
<td>Placebo + Chemo (N = 211)</td>
<td>37.9 (31.3–44.8)</td>
<td>53.6 (46.6–60.4)</td>
<td></td>
</tr>
<tr>
<td>Pembrolizumab + Chemo (N = 566)</td>
<td>41.0 (36.9–45.2)</td>
<td>56.0 (51.8–60.1)</td>
<td></td>
</tr>
<tr>
<td>Placebo + Chemo (N = 281)</td>
<td>35.9 (30.3–41.9)</td>
<td>51.6 (45.6–57.6)</td>
<td></td>
</tr>
</tbody>
</table>

ORR, % (95% CI) = Overall Response Rate
DCR, % (95% CI) = Disease Control Rate


This presentation is the intellectual property of Hope Rugo. Contact her at Hope.Rugo@ucsf.edu for permission to reprint and/or distribute.
Response Rate in Subgroups by On-Study Chemotherapy

Data cutoff December 11, 2019.

This presentation is the intellectual property of Hope Rugo. Contact her at Hope.Rugo@ucsf.edu for permission to reprint and/or distribute.

Duration of Response

Duration of response Median, mo (range)

<table>
<thead>
<tr>
<th>Group</th>
<th>PD-L1 CPS ≥10</th>
<th>PD-L1 CPS ≥1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pembrolizumab + Chemo</td>
<td>19.3 (1.6+ to 29.8)</td>
<td>10.1 (1.0+ to 29.8)</td>
</tr>
<tr>
<td>Placebo + Chemo</td>
<td>7.3 (1.5 to 32.5+)</td>
<td>6.6 (1.6 to 32.5+)</td>
</tr>
</tbody>
</table>

Duration of response Median, mo (range)

<table>
<thead>
<tr>
<th>Group</th>
<th>ITT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pembrolizumab + Chemo</td>
<td>10.1 (1.0+ to 29.8)</td>
</tr>
<tr>
<td>Placebo + Chemo</td>
<td>6.4 (1.5 to 32.5+)</td>
</tr>
</tbody>
</table>

*+* indicates there is no progressive disease by the time of last disease assessment. Data cutoff December 11, 2019.

This presentation is the intellectual property of Hope Rugo. Contact her at Hope.Rugo@ucsf.edu for permission to reprint and/or distribute.
Summary

- Pembrolizumab + chemotherapy resulted in a statistically significant and clinically meaningful improvement in PFS versus chemotherapy alone for the first-line treatment of PD-L1-positive (CPS ≥10) mTNBC
- A trend towards improved PFS with PD L1 enrichment was observed in patients treated with pembrolizumab + chemotherapy
- In subgroup analysis, PFS with pembrolizumab + chemotherapy compared to placebo + chemotherapy in patients with mTNBC was improved regardless of chemotherapy partner
- Results for the key secondary endpoints of UHK, UCK, and UUK favored pembrolizumab + chemotherapy, with the treatment effect increasing with PD-L1 enrichment
- These data further support a role for the addition of pembrolizumab to standard chemotherapy for the first-line treatment of mTNBC
- Based on the PFS results from KEYNOTE-355, pembrolizumab + chemotherapy was granted accelerated approval by the US FDA for the treatment of patients with locally recurrent unresectable or metastatic TNBC whose tumors express PD-L1 (CPS ≥10)

Zusammenfassung

- MONALEESA: Retrospektive Biomarkeranalyse der intrinsischen Subtypen zeigt keinen Effekt von Ribociclib bei basal-like Mammakarzinomen
- BYLieve: Alpelisib bei PIK3CAm und Z.n. CDK4/6i aktiv (PFS 5,7 Monate)
- HER2CLIMB:
  - Tucatinib verlängert bei HER2+ mit Hirnmetastasen Zeit zum Abfall der HR-QoL
  - Tucatinib verlängert bei HER2+ PFS und OS unabhängig vom Hormonrezeptorstatus
Zusammenfassung

- ASCENT: Nutzen durch Sacituzumab Govitecan bei TNBC unabhängig von Trop-2 Expression
- IPATunity130: Ipataserib ohne Verlängerung PFS bei PIK3CA/AKT-1/PTEN-alteriertem TNBC
- KEYNOTE-355: Pembrolizumab verlängert PFS bei TNBC mit PD-L1 CPS ≥10 unabhängig vom Chemotherapiepartner (HR 0,65; +4,1 Monate)

Save the Date: Update virtuell am 27. Februar 2021
https://www.ago2021.de