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Breast Cancer

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Moderator : Shinji Ohno (Sagara Hospital)
Discussant : Fumikata Hara (The Cancer Institute Hospital of JFCR, Department of Breast medical Oncology)

FR3-1
Japan subset Analysis in RetroBC HER2L study to Estimate the Prevalence and Describe the Clinicopathological Characteristics, Treatment Patterns, and Outcomes of HER2-Low Breast Cancer

Naoki Hayashi (Department of Breast Surgery, School of Medicine, Showa University)

FR3-2
Capivasertib (C) and fulvestrant (F) for patients (pts) with aromatase inhibitor (AI)-resistant HR+/HER2- advanced breast cancer (ABC) : Japanese subgroup analyses from the Phase 3 CAPItello-291 trial

Eriko Tokunaga (National Hospital Organization Kyushu Cancer Center)

FR3-3
Preliminary results from ASCENT-J02 : a phase (ph) 1/2 study of sacituzumab govitecan (SG) in Japanese patients (pts) with advanced solid tumors

Takahiro Kogawa (Advanced Medical Development, The Cancer Institute Hospital)

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FR3-1

Japan subset Analysis in RetroBC HER2L study to Estimate the Prevalence and Describe the Clinicopathological Characteristics, Treatment Patterns, and Outcomes of HER2-Low Breast Cancer

Naoki Hayashi [1], Eriko Tokunaga [2], Nobue Kumaki [3], Naoki Kanomata [4], Kenichi Taguchi [5], Della Varghese [6], Gareth D James [7], Shunsuke Yamazaki [8], Takehiko Takata [8], Andrew Livingston [9], Naoki Niikura [10]

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Background: About 60 % of HER2-negative (HER2-neg) breast cancers (BC) express low levels of HER2 (HER2-low; IHC 1+ or IHC 2+/ISH-). In DESTINY-Breast04, trastuzumab deruxtecan (T-DXd) showed a clinical benefit in patients (pts) with pre-treated HER2-low metastatic BC (mBC). As HER2-low becomes clinically relevant, greater understanding of it is needed. Here, we present the Japan subset analysis of RetroBC-HER2L study (NCT04807595), which assessed the HER2-low prevalence among HER2-neg mBC; described the demographics, treatment patterns and outcomes; and concordance of historical HER2 scores vs rescores, to further understand HER2-low patients in Japan.**Methods:** A Japan subset was extracted from the analysis set of the RetroBC-HER2L study and analyzed using the same objectives and methodology as that of the original study. As a prerequisite, HER2 IHC slides were rescored, blinded to historical scores, in the study.

Results: Of 798 pts enrolled overall, 155 pts were enrolled across 3 sites in Japan. Overall, HER2-low prevalence was 61.3 %; 68.3 % in hormone receptor HR+ and 37.1 % in HR-. The most frequent therapies for HER2-low in the overall treatments for metastatic setting were endocrine therapy (84.9 %) in HR+ and chemotherapy (100.0 %) in HR-. There were no notable differences in demographics, treatment patterns or clinical outcomes (HER2-low vs HER2 IHC 0). Median OS among HR+ was 35.6 months; 38.7 in HER2-low and 32.4 in HER2 IHC 0. Concordance of HER2 score was 82.6 % (kappa=0.636). The concordance pattern in this subset analysis was the same as in the main analysis, with regards to historically HER2-low being rescored as HER2 IHC 0 less often than historically HER2 IHC0 was rescored to HER2-low.**Conclusions**: HER2-low prevalence in the Japan subset was similar to that of the overall population in the RetroBC-HER2L study. The concordance results will enhance understanding of HER2-low and the importance of re-scoring with Ventana 4B5 assay designated as CDx in Japan.

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FR3-2

Capivasertib (C) and fulvestrant (F) for patients (pts) with aromatase inhibitor (AI)-resistant HR+/HER2- advanced breast cancer (ABC): Japanese subgroup analyses from the Phase 3 CAPItello-291 trial

Eriko Tokunaga [1], Hiroji Iwata [2], Mitsuya Itoh [3], Tetsuhiko Taira [4], Tatsuya Toyama [5], Toshiro Mizuno [6], Akihiko Osaki [7], Yasuhiro Yanagita [8], Seigo Nakamura [9], Rikiya Nakamura [10], Tomoko Sambe [11], Ian Wadsworth [12], Gaia Schiavon [12], Sacha J Howell [13], Masakazu Toi [14]

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Background: In the global Phase 3 CAPItello-291 trial of AI-resistant, HR+/HER2- ABC, C (a potent, selective pan-AKT inhibitor) + F significantly improved the dual primary endpoints of PFS in the overall (HR 0.60, 95 % CI 0.51-0.71; p<0.001) and AKT pathway-altered population (0.50, 95 % CI 0.38-0.65; p<0.001) vs placebo (P) + F. The most frequent grade ≥3 adverse events (AEs) were rash (group term; 12.1 %) and diarrhea (9.3 %). Here we report outcomes from pts in Japan (data cut-off Aug 15, 2022).

Methods: Pts were randomized 1:1 (stratified by liver metastases, prior use of CDK4/6 inhibitor, and region) to F (500 mg IM on days 1 and 15 of cycle 1, and day 1 of each subsequent 28-day cycle) with P or C (400 mg BID; 4 days on, 3 days off).

Results: Of the 708 pts, 78 were enrolled in Japan (C+F [37/355], P+F [41/353]). Fewer pts in Japan vs the global population had liver metastases (30.8 % vs 43.2 %) or had received a CDK4/6 inhibitor (mostly due to preference; 16.7 % vs 70.1 %) or prior endocrine therapy for advanced/metastatic disease (65.4 % vs 86.9 %), while a higher proportion had ECOG PS 0 (89.7 % vs 65.7 %).

Median PFS was 13.9 mo with C+F vs 7.6 mo with P+F (HR 0.73, 95 % CI 0.40-1.28) and was 13.9 vs 9.1 mo in pts with AKT alterations (n=38; HR 0.65, 95 % CI 0.29-1.39). Relative PFS benefit was consistent with the global population, although median PFS was longer in both arms, likely due to demographic differences.

Safety of C+F in pts from Japan was broadly similar to the global population; diarrhea was the most frequent AE (73.0 % vs 22.0 % P+F). The most frequent grade ≥3 AEs with C+F were rash (group term; 18.9 % [predominantly rash maculopapular; 16.2 %] vs 0 % P+F), diarrhea, and drug eruption (both 10.8 % vs 0 %). AEs leading to discontinuation of C/P were reported in 24.3 % for C and 0 % for P.

Conclusions: The benefit-risk profile of C+F in pts in Japan reflects the global CAPItello-291 population; no new safety concerns with C+F specific to Japanese pts were identified.

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FR3-3

Preliminary results from ASCENT-J02：a phase (ph) 1/2 study of sacituzumab govitecan (SG) in Japanese patients (pts) with advanced solid tumors

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Background: SG is an antibody-drug conjugate comprising an anti-Trop-2 antibody coupled to a potent SN-38 payload. Based on results from the ASCENT, TROPiCS-02, and TROPHY studies, SG is FDA-approved for second line or later treatment (tx) of locally advanced or metastatic urothelial cancer, triple negative breast cancer and HR+/HER2- breast cancer. ASCENT-J02 (NCT05101096) is an open-label, ph 1/2 study of SG in Japanese pts with advanced solid tumors. We report ph 1 safety and pharmacokinetics.

Methods: Pts in cohort A (wild-type *UGT1A1*) received intravenous SG 6mg/kg escalating to 10mg/kg on Days 1 and 8 of a 21-day cycle using a 3+3 design to assess dose-limiting toxicity (DLT) and determine recommended ph 2 dose (RP2D). Then, pts in cohort B (heterozygous or homozygous *UGT1A1** 28, *UGT1A1** 6) received SG 6mg/kg; next dose level in cohort B began after 21-day safety run-in. Primary objectives: safety and RP2D. Serum concentration-time profiles of SG, total antibody, total SN -38, and free SN-38 were evaluated.

Results: Six pts (3 in cohort A, 3 in B) received SG 6mg/kg and 9 (6 in cohort A, 3 in B) received SG 10mg/kg; 8 pts (53 %) had breast cancer; median age, 49y (range 37-73) ; 73 % female. One DLT of grade (G) 3 elevated transaminases occurred with 10 mg/kg in cohort A. RP2D was SG 10 mg/kg. At readout time, 4 pts discontinued due to disease progression; 2 each in SG 6 and 10mg/kg. G3 tx-related adverse events (TRAEs) were neutropenia (1 [17 %] in SG 6mg/kg; 5 [56 %] in 10mg/kg) and leukopenia (3 [33 %] in 10mg/kg). No gastrointestinal G ≧ 3 TRAEs occurred. One pt (11 %) had a G4 TRAE of neutropenia in 10mg/kg. Dose-dependent increase in SG and free SN-38 serum exposure was observed. At 10mg/kg, median terminal half-life of SG was ~ 23h, and for free SN-38 it was ~ 19h.

Conclusion: SG 10mg/kg tolerability and serum exposure in Japanese pts was consistent with known safety and exposure profiles, with no new safety concerns. SG RP2D was 10mg/kg; ph 2 part is ongoing.

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