**Tumor responses**

Tumor lesions were assessed by computed tomography or magnetic resonance imaging within 28 days before enrollment (baseline) and then every 8 weeks the first year, every 12 weeks thereafter. Response was assessed by the investigator based on RECIST v1.1.

**Safety**

Safety parameters included the incidence of treatment-emergent adverse events and serious adverse. Treatment-emergent adverse events were defined as events that emerges during treatment, having been absent pre-treatment, or worsens relative to the pretreatment state during the study treatment and up to 30 days after the last dose of the therapeutic drug or discontinuation of the clinical trial, whichever is later. Serious adverse were collected up to 30 days after the last dose of trial treatment.

Adverse events were documented and evaluated based on the National Cancer Institute Common Terminology Criteria for Adverse Events (version 5.0) Data. All AEs occurring during the study period were followed until resolution, stabilization, or subsequent treatment or death. All AEs were characterized by severity and whether they were related to the study drug.

DLTs were evaluated during the first 4 weeks as the DLT evaluation period. DLTs were defined as any of the following toxicities determined to be caused as a result of study treatment: grade 4
hematologic toxicity lasting $\geq$ 7 days, grade 3 $\geq$ febrile neutropenia, nonhematologic toxicity of grade $\geq$ 3 (despite of nausea, vomiting, diarrhea, electrolyte abnormalities), nausea, vomiting, and diarrhea of grade $\geq$ 3 despite maximal supportive care, and toxicities that resulted in administration of $< 50\%$ of the planned abemaciclib or endocrine therapy dose. Once the initiation of treatment in the sixth case is confirmed, new enrollment in the study will be temporarily halted, and a safety assessment will be conducted by the Coordinating Committee to determine whether the study can be continued.

**Sample collection and preparation**

Archival, formalin-fixed, paraffin-embedded (FFPE) tumor tissue was obtained after informed consent before the protocol treatment. Liver biopsy was performed for three subjects upon severe hepatotoxicity $\geq$ grade 3, and the physician deemed it necessary for diagnosis. Their archival FFPE tissues were provided for the study. Blood samples were collected before treatment, on day 15 of cycle 1, day 1 of cycle 2, day 1 of cycle 3, day 1 of cycle 8, and end of the treatment (supplementary table 1). Blood samples were also collected at the onset of irAE and disease progression. For peripheral blood mononuclear cell (PBMC) preparation, the supernatant was separated via centrifugation at 1500xg for 15 min at room temperature. The pellet was resuspended in phosphate-buffered saline (PBS) and washed twice with PBS. The
isolated PBMCs were stored in BAMBANKER (GC LYMPHOTEC, Tokyo, Japan) at −80 °C and then in liquid nitrogen until further analysis. The blood sample for serum was kept at room temperature for 30 minutes. Then, serum was isolated by centrifugation at 1,500×g for 15 mins at room temperature. Plasma was isolated within 2 hours of blood collection by centrifugation at 1,900×g for 10 mins at room temperature. The buffy coat was collected after the first centrifugation. Plasma and buffy coat were stored at −80°C until use. Stool samples were obtained from the patients on day 1 of the first and third cycles and suspended in a solution including guanidine, and sent at room temperature.

**PD-L1 assay in tumor tissues**

Tumor samples were fixed in 10% buffered formalin and embedded in paraffin following standard procedures at each study site. Immunohistochemistry of PD-L1 was performed with Ventana OptiView PD-L1(SP142). Two pathologists evaluated immune-stained sections from 17 subjects before the protocol treatments and scored PD-L1 according to the Ventana Optiview PD-L1 (SP142) guide. Tumor-infiltrating immune cells (IC) are evaluated by determining the proportion of the tumor area occupied by PD-L1 staining IC, regardless of the intensity. To confirm PD-L1 expression, a specimen should show ≥ 1% IC. If the specimen demonstrates PD-L1 staining of any intensity in IC, covering ≥ 1% of the tumor area, it will be classified as
having a PD-L1 expression level of ≥ 1% IC. IC are immune cells in the intratumoral and contiguous peritumoral stroma, including lymphocytes, macrophages, and cells with dendritic or reticular morphology. Negative reagent controls were evaluated in each case to confirm acceptable background staining. Staining intensity was not part of the evaluation.

**Genotyping of human leukocyte antigen (HLA) and ATP binding cassette subfamily G member 2 (ABCG2)**

In this post-hoc analysis, genomic DNA was extracted from the stored PBMC at −80 °C. Seven HLA genes (HLA-A, -B, -C, -DRB1, -DPB1, -DQA1, and -DQB1) were genotyped by next generation sequencing method. ABCG2 421C>A was genotyped by PCR-Invader method.

**Tumor subtype classification**

The tumor samples before the treatment were classified using the molecular subtype by Oncocyte Corporation Transcriptome libraries, which were constructed using a TruSeq RNA Exome Library Prep Kit (Illumina, San Diego, CA) using 100 ng of total RNA extracted from FFPE tissue sections according to the manufacturer’s recommendations. Libraries were sequenced on an Illumina NextSeq 500 with 150 paired-end cycles and a mean of 25 million reads per sample. Transcripts were aligned to the human reference assembly GRCh37
(Ensembl) using the STAR application (v. 020201). Assembly and expression quantification were performed using Cufflinks tools (v. 2.2.1). The resulting FPKM data for each sample were compiled and analyzed with the TNBCtype-IM algorithm. Determa IO™ test measures 27-genes to assess the entire tumor immune microenvironment. The IO score calculated by Determa IO™ test has been validated as a biomarker that identifies patients likely to benefit from ICIs in TNBC and NSCLC.²³

References


