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News Release

2014 年 12 月 10 日

アステラス製薬　経口アンドロゲン受容体阻害剤エンザルタミド サンアントニオ乳癌シンポジウム（SABCS）でのデータ発表に関するお知らせ

アステラス製薬株式会社（本社：東京、社長：畑中 好彦、以下「アステラス製薬」）は、米国メディベーション社と共同で開発・商業化を進めている経口アンドロゲン受容体阻害剤エンザルタミド（一般名、製品名：XTANDI®、開発コード：MDV3100）に関し、アンドロゲン受容体陽性のトリプルネガティブ進行再発乳がん患者を対象に、エンザルタミド単剤療法の有用性を検討する第II相臨床試験のデータが、サンアントニオ乳癌シンポジウム（SABCS：San Antonio Breast Cancer Symposium）の第 37 回 年次総会（開催時期：12 月 9 日～13 日、開催場所：テキサス州サンアントニオ）で発表されますので、お知らせします。

アブストラクトは以下の通りです。なお、ポスターセッションは現地時間 12 月 12 日（金）午後 5 時からを予定しています。

[P5-19-09] Stage 1 results from MDV3100-11: A 2-stage study of enzalutamide (ENZA), an androgen receptor (AR) inhibitor, in advanced AR+ triple-negative breast cancer (TNBC)

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Background

TNBC is a heterogeneous disease with many subtypes that share one commonality; "triple-negative" breast tumors lack sufficient expression of a target (ER, PgR, HER2) associated with a therapeutic agent. AR expression occurs in a subset of TNBC and could identify patients (pts) that respond to AR inhibition. Preclinically, AR+ TNBC cell lines grow in response to AR stimulation and this growth is inhibited by ENZA. A phase 2 clinical study investigating bicalutamide in AR+ TNBC demonstrated a 19% clinical benefit rate at 24 weeks (CBR24) with no objective responses in 24 pts. ENZA is a potent AR inhibitor that improves overall survival in men with metastatic castration-resistant prostate cancer and is being evaluated in pts with advanced AR+ TNBC.

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Methods

MDV3100-11 is an open-label, Simon 2-stage study evaluating ENZA (160 mg daily) in pts whose breast cancer expresses AR (>0% by IHC) but not ER, PgR or HER2 amplification (NCT01889238). There was no limit to prior therapies; bone-only non-measurable disease was allowed. Pts with CNS metastases or seizure history were excluded. Tissue was required; prescreening for AR was allowed. The primary endpoint is CBR at 16 weeks (CBR16), defined as complete response (CR), partial response (PR), or stable disease (SD) ≥16 weeks per RECIST 1.1 in Evaluable pts. Evaluable pts were prespecified as those with tumors expressing ≥10% AR by central review *and* who had assessment for response. ITT analyses include all pts. Secondary endpoints include CBR24, response rates, safety and tolerability. The analysis plan specified progression to Stage 2 if CBR16 is ≥3 of 26 Evaluable pts in Stage 1, and the null hypothesis (true CBR16=8%) is rejected if overall CBR16 is ≥9 in 62 Evaluable pts.

Results

Complete data on all Stage 1 pts (N=42) are reported herein; 16 were not evaluable (10 had AR <10%, 6 had AR ≥10% but no response assessment). In the 26 Evaluable pts, median age was 62.5 years, 77% had measurable disease, 69% had ≥3 sites of metastases, 62% had visceral involvement, and 42% received ENZA in ≥3rd line. CBR16 was 42% (11 of 26; 95%CI 24, 62) and CBR24 was 35% (9 of 26; 95%CI 18, 54), with 1 PR and 1 CR. Related adverse events (AEs) of any grade ≥10% in the ITT were fatigue (29%), nausea (26%), decreased appetite (19%), diarrhea (14%), hot flush (12%) and vomiting (10%). Fatigue (7%) was the only Grade ≥3 related AE in ≥5%. Go to Stage 2 criteria were met, and enrollment is complete at 118. As of Sept 2014, 13 additional pts had clinical benefit at week 16 (including 3 PRs); data continue to mature.

Conclusion

The 42% CBR16 observed in Stage 1 alone was sufficiently high to reject the null hypothesis for the whole study. Data beyond Stage 1 are not mature; however, responses continue to be observed. AEs from ENZA in women with TNBC were generally mild and consistent with other studies of ENZA. These encouraging results suggest ENZA may provide meaningful benefit to pts with AR+ TNBC. Ongoing IHC and genomic analyses on 400 collected tissue samples will further inform how best to identify pts most likely to derive benefit from ENZA.

Poster Session: Advanced Therapy - Targeted (Friday, December 12, 2014 5:00 PM)

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