# BRAND NAME™ (Drug X) – Use in Patients With Brain Metastases

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## SUMMARY


- BRAND NAME is not indicated as a treatment for brain metastases, breast cancer, and/or leptomeningeal carcinomas.

- BRAND NAME is indicated to treat cancer progressing after platinum-based chemotherapy.

- Four clinical trials from the TAYLOR Clinical Trial Program (ie, TAYLOR-2, TAYLOR-3, TAYLOR-6, and TAYLOR-7) included patients with cancer having brain metastases. Because only a small number of patients in the individual trials had brain metastases, an exploratory combined analysis of a patients with cancer having brain metastases from the TAYLOR-3 and TAYLOR-6 trials was conducted to increase the sample size.
    - In TAYLOR-2 trial, ORR with Drug X did not significantly differ between patients with and without brain metastases. Safety results were not stratified based on the presence or absence of brain metastases. In the overall population, the most commonly reported drug-related adverse events were diarrhea and skin-related adverse events.
    - In the TAYLOR-3 and TAYLOR-6 trials, PFS and OS in patients with brain metastases did not significantly differ between Drug X- and chemotherapy-treated patients; however, ORR was significantly improved with Drug X. In the combined analysis of the TAYLOR-3 and TAYLOR-6 trials, PFS but not OS was significantly improved with Drug X. In these trials, safety results were not stratified based on the presence or absence of brain metastases. In the overall population from the TAYLOR-3 trial, the most commonly reported treatment-related adverse events with Drug X were diarrhea, rash, and dryness/irritation of the skin, mucosa, and nails. In the overall population from the TAYLOR-6 trial, most common reported treatment-related grade 3/4 AEs with Drug X were rash/acne, diarrhea, and stomatitis/mucositis.


## CLINICAL DATA

The information summarized below is not intended to be all-inclusive, but rather a concise summation of relevant clinical data.

A search of the published biomedical literature identified clinical trials and case studies that evaluated the use of Drug X in patients with brain metastases. The majority of available data were from patients with cancer. Some data from patients with other tumor types, including breast cancer and leptomeningeal carcinomas, were also reported.

### Taylor Clinical Trial Program

The TAYLOR Clinical Trial Program evaluated the use of Drug X in patients with cancer. Several TAYLOR-trials (ie, TAYLOR-2, TAYLOR-3, TAYLOR-6, and TAYLOR-7) have reported results in patients with brain metastases.[1,2,3,4] Because only a small number of patients in the individual trials had brain metastases, an exploratory combined analysis of a patients with cancer having brain metastases from the TAYLOR-3 and TAYLOR-6 trials was conducted to increase the sample size.

| TAYLOR-2 | TAYLOR-3 | TAYLOR-6 | TAYLOR-7 |
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**TAYLOR-2:** This single-arm, Phase II study evaluated Drug X in patients with EGFR-positive lung adenocarcinoma.1

Methods:

- Of the 129 patients enrolled in this trial, 31 patients had asymptomatic brain metastases at baseline.
- Prespecified subgroup analyses included patients with and without brain metastases.
- The primary endpoint was ORR (assessed via RECIST version 1.0). Safety was also assessed.

Efficacy Results:

- ORR did not significantly differ based on the presence or absence of brain metastases (65% vs. 60%, respectively).

Safety Results:

- Safety results were not stratified based on the presence or absence of brain metastases.
- In the overall population of patients:
  - A total of 128 of 129 patients had drug-related AEs.
  - The most commonly reported drug-related AEs were diarrhea and skin-related AEs.
  - The occurrence of diarrhea and skin-related AEs was lower with the 40-mg dose.
  - Treatment-related serious AEs were reported in 16 patients (40-mg starting dose, n=2; 50-mg starting dose, n=14).
  - ILD was reported in 4 patients; 1 of these events was fatal. There were no other potentially treatment-related deaths.

**TAYLOR-3:** This Phase III, randomized trial compared Drug X to cisplatin in patients with EGFR-positive, metastatic lung adenocarcinoma.2

Methods:

- Patients were randomized 2:1 to either (1) Drug X 40 mg orally once daily or (2) cisplatin 75 mg/m$^2$ IV plus pemetrexed 500 mg/m$^2$ IV once every 21 days up to a maximum of 6 cycles.
- Of the 345 patients who were randomly assigned, 35 patients had asymptomatic brain metastases at baseline.
- The primary endpoint was PFS (assessed via independent blinded review). Safety was also assessed.

Efficacy Results:

- PFS in patients with brain metastases did not significantly differ between treatment groups; the median PFS was 11.1 months with Drug X and 5.4 months with chemotherapy. The magnitude of PFS improvement with Drug X vs. chemotherapy was similar to that observed in patients without brain metastases.
- OS in patients with brain metastases did not significantly differ between treatment groups; the median OS was 19.8 months with Drug X and 33.2 months with chemotherapy.
- ORR in patients with brain metastases having common EGFR mutations was significantly improved with Drug X vs. chemotherapy (p=0.0058).

Safety Results:

- Safety results were not stratified based on the presence or absence of brain metastases.

- In the overall population of patients:
  - Treatment-related AEs grade ≥3 were reported in 195 patients (Drug X, n=112; chemotherapy, n=53 patients).
  - The most commonly reported treatment-related AEs with Drug X were diarrhea, rash, and dryness/irritation of the skin, mucosa, and nails, whereas the most commonly reported treatment-related AEs with chemotherapy were decreased appetite, fatigue, nausea/vomiting, and myelosuppression.
  - ILD-like disease was reported in 3 patients.
- There were 4 potentially treatment-related deaths among those receiving Drug X, whereas there were none with chemotherapy.

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**TAYLOR-6:** This Phase III, randomized, open-label trial compared Drug X to chemotherapy as first-line treatment of patients with EGFR-positive, Stage IIIB or IV lung adenocarcinoma.3

Methods:

- Patients were randomized 2:1 to either (1) Drug X 40 mg orally once daily or (2) gemcitabine 1000 mg/m² IV on Day 1 and Day 8 plus cisplatin 75 mg/m² IV on Day 1 of a 3-week schedule for up to six cycles.3
- Of the 364 patients who were randomly assigned, 46 patients had asymptomatic brain metastases at baseline
- The primary endpoint was PFS (assessed via independent review). Safety was also assessed.3

Efficacy Results:

- PFS in patients with brain metastases did not significantly differ between groups; the median PFS was 8.2 months with Drug X and 4.7 months with chemotherapy.
- OS in patients with brain metastases did not significantly differ between groups; the median OS was 22.4 months with Drug X and 24.7 months with chemotherapy.
- ORR in patients with brain metastases having common EGFR mutations was significantly improved with Drug X vs. chemotherapy (p=0.0027).

Safety Results:

- Safety results were not stratified based on the presence or absence of brain metastases.
- In the overall population of patients:
  - Treatment-related AEs grade ≥3 were reported in 154 patients (Drug X, n=86; chemotherapy, n=68).
  - The most common reported treatment-related grade 3/4 AEs with Drug X were rash/acne, diarrhea, and stomatitis/mucositis; the most commonly reported treatment-related grade 3/4 AEs with chemotherapy were neutropenia, nausea, vomiting, and leucopenia.
    - One patient in each group died. Both deaths were considered potentially treatment-related (sudden death with Drug X and cardiac failure with chemotherapy) in 3 patients.
    - There were 4 potentially treatment-related deaths among those receiving Drug X, whereas there were none with chemotherapy.

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**TAYLOR-7:** This Phase IIB, exploratory, randomized, controlled, open-label trial compared Drug X 40 mg orally once daily to Drug Y 250 mg orally once daily as first-line treatment of patients with EGFR-positive cancer.4

Methods:

- Of the 319 patients enrolled in this trial (Drug X, n=160; Drug Y, n=159), 50 patients had brain metastases at baseline (Drug X, n=26; Drug Y, n=24). Randomization was stratified by status of brain metastases.
- Coprimary endpoints were PFS (assessed via independent central review), TTF, and OS. Safety was also assessed.

Efficacy Results:

- The differences in PFS and TTF between the Drug X and Drug Y groups for the whole study population were largely unaffected by the presence or absence of brain metastases.
- In patients with brain metastases, the median PFS was 7.2 months with Drug X and 7.4 months with Drug Y. In patients without brain metastases, the median PFS was 12.7 months with Drug X and 10.9 months with Drug Y.
- In patients with brain metastases, the median TTF was 8.4 months with Drug X and 9.3 months with Drug Y. In patients without brain metastases, the median PFS was 14.5 months with Drug X and 11.6 months with Drug Y.

Safety Results:

- Safety results were not stratified based on the presence or absence of brain metastases.
- In the overall population of patients:
  - The overall frequency and severity of all-cause AEs were similar between Drug X and Drug Y.
  - The most frequently reported grade ≥3 AEs with Drug X were diarrhea, rash/acne, and fatigue; whereas, the most commonly reported grade ≥3 AEs with Drug Y were increased AST and ALT concentrations, and rash/acne.

## ABBREVIATIONS

AE, adverse event; ALT, alanine aminotransferase; AST, aspartate aminotransferase; CNS, central nervous system; EGFR, epidermal growth factor receptor; HER-2, human epidermal growth factor receptor 2; ILD, interstitial lung disease; IV, intravenous; ORR, objective response rate; OS, overall survival; PFS, profession-free survival; RECIST, Response Evaluation Criteria In Solid Tumors; TTF, time to treatment failure.

## REFERENCES


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[4] Antonia S, Goldberg SB, Balmanoukian A, et al. Safety and antitumour activity of durvalumab plus tremelimumab in non-small cell lung cancer: a multicentre, Phase 1B study. *Lancet Oncol*. 2016;17:299-308.