**Commercially Successful Antibody-Drug Conjugates for Cancer Treatment**

Sung Min Kim, **Jin Woo Park,** Sang Woo Kim, Kwan Hyung Cho.

Department of Pharmacy, Inje University, Gimhae, Gyeongsangnam-do, Republic of Korea.

**Background and aims.** The increasing incidence of cancers, including breast cancer, and the emergence of resistance to current therapies highlight the need for novel treatment strategies. Antibody-drug conjugates (ADCs) are a promising class of targeted cancer therapies that combine the specificity of monoclonal antibodies with the efficacy of cytotoxic agents. Currently, 15 ADCs have been approved worldwide, with breast cancer being the most common indication. This study aims to analyze commercially successful ADCs.

**Methods.** We examined ADCs targeting breast cancer, which account for approximately 60% of total ADC sales. Among them, three key ADCs, Kadcyla, Enhertu, and Trodelvy were selected for analysis.

**Results.** Kadcyla, approved in 2013, was initially the top-selling ADC but demonstrated efficacy only in patients with HER2-positive metastatic breast cancer (mBC). To address this limitation, Enhertu (approved in 2019) and Trodelvy (approved in 2020) were developed. Enhertu demonstrated efficacy in both HER2-positive and HER2-low patients, thereby expanding the eligible patient population. Trodelvy has shown effective in HER2-negative cases, including triple-negative breast cancer (TNBC), HR-positive and HER2-negative subtypes. Among the three agents, Enhertu demonstrated superior clinical outcomes. Enhertu demonstrated a 3-fold increase in median progression-free survival (mPFS), an improvement of approximately 7% in 24-month overall survival (OS), and a 50% higher overall response rate (ORR) compared to Kadcyla. In addition, approximately 21% of patients achieved a complete response (CR), indicating complete tumor disappearance in one out of five cases. Reflecting its demonstrated efficacy, Enhertu achieved global sales of $2.566 billion as of 2023, surpassing Kadcyla.

**Conclusion/Discussion.** While ADCs represent a promising strategy for effective cancer treatment, several challenges remain, including optimizing ADC selection, broadening efficacy across tumor types, and overcoming resistance mechanisms. Continued research and clinical trials are required to achieve the therapeutic potential of ADCs in improving the safety and efficacy of cancer treatment.

**Acknowledgement.** This research was supported by the Basic Science Research Program through the National Research Foundation of Korea (NRF) funded by the Ministry of Science, ICT & Future Planning (Grant number: NRF-2022R1A2C1003070).

**References:**

(1) Song, C. H. et al (2023) Antibodies 12(4):72

(2) Chen, Y. F. et al (2023) Cancer Communications 43(3):297-337