Sipuleucel-T (Provenge®): autopsy of an innovative change of paradigm in cancer treatment

Jarosławski S1, Caban A1, Touni M2
1Creativ-Ceutical, Kraków, Poland; 2Aix-Marseille University, Marseille, France

BACKGROUND
• Prostate cancer is the second most common cancer in men in the USA, after skin cancer.
• The intravenous therapeutic vaccine sipuleucel-T (Provenge®) was introduced in the USA in May 2010 for asymptomatic patients with metastatic, castration-resistant prostate cancer (mCRPC) prior to chemotherapy.
• It is prepared individually for each patient and infused in three sessions over a period of one month. Sipuleucel-T was the first therapeutic vaccine to treat cancer, first alternative to chemotherapy for metastatic prostate cancer patients with few side effects and first biological and personalised treatment for prostate cancer.
• Sipuleucel-T failed to achieve commercial success in the USA and Europe. Five years after its launch in the USA, the company behind the vaccine, Dendreon, filed for bankruptcy and was acquired by a larger pharmaceutical company. While the drug is still offered in the USA, it was withdrawn from the European market for commercial reasons merely a few months after obtaining its European marketing authorization.

OBJECTIVES
• To review probable causes for why Sipuleucel-T failed to achieve commercial success in the USA and Europe.

METHODS
• PubMed and Google searches were performed to inform this material. The inclusion criteria were defined as any literature on sipuleucel-T that would reflect clinical, healthcare management, market access, pricing, health technology assessment (HTA), and business points of view in both the US and European markets. The following queries were used for both searches: (reimbursement OR coverage OR payment OR payers OR cost OR price OR pricing OR cost-effectiveness OR Medicare OR CMS) AND (provence OR sipuleucel-T) on 1 June 2015. The abstracts of all PubMed results and the titles of the first 200 Google hits were screened for relevance. Pharmaceutical industry websites were also screened for materials.

APPROVAL
• The US Food and Drug Administration (FDA) rejected Dendreon’s first application for sipuleucel-T in May 2007 [1]. This was because advanced-stage cancer treatments do not typically extend survival, but merely stop the tumor progression. Sipuleucel-T, however, had the opposite effect of extended survival, with no measurable tumor shrinkage [2].
• In its pivotal phase III trial requested by the FDA sipuleucel-T extended survival by four months as compared to placebo (25.8 months versus 21.7 months).
• Sipuleucel-T was cleared by FDA in 2010 and by the European Medicines Agency in 2013, but other agencies were not approached.

PRICING & REIMBURSEMENT
• Sipuleucel-T was priced at US$ 93,000 for a 1-month course of treatment.
• The high price, political pressure, doubts about the vaccine’s effectiveness and classification led the US Centers for Medicare and Medicaid Services (CMS) to launch a 1-year National Coverage Determination procedure.
• Despite a final positive reimbursement decision, this resulted in another year of delay in accessing the market [3].
• UK and German HTA bodies did not recommend reimbursement.

ADOPTION BY DOCTORS AND PROVIDERS
• The vaccine’s supply in the US was limited during the first year of launch due to a small manufacturing capacity [4].
• Despite a positive recommendation by the National Comprehensive Cancer Network, sipuleucel-T’s complex administration, high price, and uncertainty about the reimbursement status caused stagnation of sales [4].
• The high up-front cost and lack of a marker to assess response to treatment deterred many doctors from prescribing the vaccine.
• In addition, two cheaper, oral metastatic prostate cancer drugs with similar survival benefits and a possibility to monitor response reached the US market one and two years after sipuleucel-T [5].

FINANCIAL PROBLEMS
• Faced with stagnant sales and the arrival of competitors, a few CEOs attempted to rescue the company from soaring debts by reducing the cost and substantial staff reductions.
• Even though Dendreon’s market capitalization topped US$ 7.5 billion following the FDA’s approval of sipuleucel-T, this value degraded gradually until the firm’s bankruptcy five years later.

CONCLUSIONS
• The cause of Dendreon’s bankruptcy was multi-factorial (Figure 1), of which two issues contributed the most: the delay in securing FDA approval and CMS coverage, and the very high price that had to be incurred by providers up-front. In practice, the product was characterized by many potential barriers to market access, such as a mechanism of action previously unknown to the FDA, EMA or CMS; high up-front costs; complex administration; limited manufacturing capacity; no markers of treatment response; and soon-to-arrive competitor drugs.
• The poor market access experienced by the single-product biotech company implies it may have benefited from a support of a strong regulatory and market access advisory partner.