Ibrutinib

Ibrutinib (Imbruvica) is a small molecule drug that binds permanently to a protein, Bruton's tyrosine kinase (BTK), that is important in B cells; the drug is used to treat B cell cancers like mantle cell lymphoma, chronic lymphocytic leukemia, and Waldenström's macroglobulinemia, a form of non-Hodgkin's lymphoma.

Ibrutinib was created by scientists at Celera Genomics as a tool compound for studying BTK function, then developed by Pharmacyclics up to Phase II, then partnered with Johnson & Johnson. Pharmacyclics was acquired by AbbVie in May 2015, and Abbvie projected global sales of US$1 billion in 2016 and $5 billion in 2020.

According to the Wall Street Journal in January 2016 ibrutinib, a specialty drug, cost US$116,600 to $155,400 a year wholesale in the United States. In spite of discounts and medical insurance, the prohibitive price causes some patients to not fill their prescriptions.

A study evaluated the efficacy of ibrutinib administration in the acute phase of SCI on neural tissue preservation and locomotor recovery. Ibrutinib was delivered intravenously at 3.125 mg/kg either immediately, 12 hours after, or both immediately and 12 hours after SCI induction in adult male C57BL/6 mice. Neutrophil influx into the lesion area was evaluated 24 hours following SCI using light microscopy and immunohistochemistry methods. Animals' body weight changes were recorded, and their functional motor recovery was assessed based on the Basso mouse scale during 28 days after treatment. Finally, spinal cord lesion volume was estimated by an unbiased stereological method. While animals' weight in the control group started to increase one week after injury, it stayed unchanged in treatment groups. However, the double injection of ibrutinib led to significantly lower body weight compared to the control group at 4 weeks post-injury. Mean neutrophil counts per visual field and the lesion volume were significantly decreased in all ibrutinib-treated groups. In addition, ibrutinib significantly improved locomotor functional recovery in all treated groups, especially in immediate and double-injection groups. Neural tissue protection and locomotor functional recovery suggest ibrutinib treatment as a potent immunotherapeutic intervention for traumatic SCI that warrants clinical testing [1)].

Ibrutinib selectively targeted neoplastic pericytes and disrupted the BTB, but not the BBB, thereby increasing drug effusion into established tumors and enhancing the chemotherapeutic efficacy of drugs with poor BTB penetration. These findings highlight the clinical potential of targeting neoplastic pericytes to significantly improve treatment of brain tumors [2)].

Ibrutinib exerts a profound antitumor effect and induces autophagy through Akt/mTOR signaling pathway in Glioblastoma cells. Autophagy inhibition promotes the antitumor activity of ibrutinib in Glioblastoma. Our findings provide important insights into the action of an anticancer agent combining with autophagy inhibitor for malignant glioma [3)].

Hemorrhagic events were reported in the original trials, however the mechanism of bleeding is just being elucidated. Recent studies have demonstrated platelet dysfunction as a mechanism of bleeding. Currently we report two patients who developed life-threatening central nervous system hemorrhage while receiving ibrutinib for chronic lymphoid leukemia (CLL) and mantle cell lymphoma, respectively. Both patients improved rapidly after platelet transfusions even though their platelet counts were normal or only mildly reduced at the time of hemorrhage. We suggest that platelet transfusions can ameliorate the platelet dysfunction defect of ibrutinib and can support the patient through the critical period until new platelet production occurs [4].

A patient received ibrutinib and had a complete response at 3 months, which was maintained to the present (6 months). After a review of the literature, González-Bonet et al. found different pathologies that can mimic subdural hematomas. However, this is the first report of a lymphoma with CNS involvement mimicking bilateral subdural hematomas. This report contributes to the knowledge of lymphomas with CNS involvement. Its strange radiographic appearance and histologic type make it unique [5].

1)
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