Preliminary Clinical Response of Ribociclib as Single Agent in Advanced Breast Cancer: In Search of New Therapeutic Indications

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Background

Ribociclib an orally bioavailable, highly specific inhibitor of CDK4/6, is currently approved in combination with an aromatase inhibitor for the treatment of pre/perimenopausal women with HR-positive, HER2-negative advanced breast cancer. Alterations in the CDK4/6-Rb-E2F pathway, which promotes cell proliferation, usually occur in human tumors. Thus, Ribociclib remains as an attractive therapeutic strategy for the treatment of other neoplasms in which this pathway is significantly dysregulated.

Purpose

Evaluate preliminary clinical response of Ribociclib as a single agent, in terms of Best Overall Response (BOR) and Progression-Free Survival (PFS), in patients with Rb+ advanced solid tumors (AST) and lymphomas.

Design

Literature Review

Studies published during **2016-2019**

Electronic databases **Medline, Embase,** and **Cochrane Library**

No restrictions in terms of language or publication year were applied

Search strategy terms were: **“clinical response”**, **“Ribociclib”**, **“single-agent”**, **“advanced cancer”**. Boolean operators were used to connect specific search keywords for each database and other free-text terms.

Results

5 Clinical trials were found

NCT01237236 Phase I: 132 patients Europe and US with Rb+ AST and Lymphomas. Ribociclib showed preliminary signs of clinical activity. 3 patients achieved Partial Response (PR), 43 a BOR of Stable Disease (SD) and 8 had PFS for >6 months.

NCT01237236 Phase I: 17 Japanese patients with advanced esophageal, breast, peritoneum and soft tissue tumors. Ribociclib exhibited limited response, as no patients achieved Complete Response (CR) or PR, and 4 achieved BOR on SD.

NCT01747876 Phase I: 32 pediatric patients with neuroblastoma and malignant rhabdoid tumors. BOR was SD in 9 patients and 5 achieved SD for more than 6,6,8,12 and 13 cycles, respectively.

NCT02933736 Phase 0 and NCT02345824 Phase Ib assessed Ribociclib clinical response as monotherapy in glioblastoma. Results showed limited clinical efficacy and ineffectiveness, respectively. Both studies mentioned the presence of a significant increase in cells mTOR/PI3K signaling pathway activity.

Conclusion

Inhibition of CDK4/6-Rb-E2F pathway by Ribociclib showed **preliminary limited clinical response** in patients with **AST and lymphomas**. However, observation of prolonged SD support further investigation of Ribociclib combination with other agents, specially with mTOR/PI3K inhibitors.

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