Everolimus

Everolimus (INN) (earlier code name RAD001) is the 40-O-(2-hydroxyethyl) derivative of sirolimus and works similarly to sirolimus as an mTOR inhibitor.

It is currently used as an immunosuppressant to prevent rejection of organ transplants and treatment of renal cell cancer and other tumours. Much research has also been conducted on everolimus and other mTOR inhibitors as targeted therapy for use in a number of cancers.

It is marketed by Novartis under the tradenames Zortress (USA) and Certican (Europe and other countries) in transplantation medicine, and Afinitor in oncology. Everolimus also available with Biocon with the brand name of Evertor.

Loss of PTEN function in glioblastoma (Glioblastoma) leads to increased AKT activity which activates the mammalian target of rapamycin (mTOR) through TSC1/2 and Rheb. mTOR inhibitors reduce tumor cell proliferation and tumor growth. Baselga et al. in a landmark phase III trial (which randomized advanced hormone receptor positive breast cancers to everolimus plus exemestane versus exemestane plus placebo) showed a significant improvement in median PFS with the addition of everolimus (10.6 vs. 4.1 months). Drawing from the success of mTOR inhibitors in breast cancers, Hainsworth et al. evaluated the impact of VEGF inhibitor with everolimus (an mTOR inhibitor) when combined with standard radiation therapy and TMZ for newly diagnosed Glioblastoma. Median PFS was 11.3 months, and median OS was 13.9 months. Patients experienced the class side effects of mTOR inhibitors as well as VEGF inhibitors without much improvement in outcome¹⁾.

Everolimus for subependymal giant cell astrocytoma

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1)

Mallick S, Gandhi AK, Rath GK. Therapeutic approach beyond conventional temozolomide for newly diagnosed glioblastoma: Review of the present evidence and future direction. Indian J Med Paediatr Oncol. 2015 Oct-Dec;36(4):229-37. doi: 10.4103/0971-5851.171543. Review. PubMed PMID: 26811592; PubMed Central PMCID: PMC4711221.

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