Interleukin-2
A Review of its Pharmacological Properties and Therapeutic Use in Patients with Cancer

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Summary

Recombinant interleukin-2 (IL-2) products (e.g. aldesleukin, teceleukin) are nonglycosylated, modified forms of the endogenous compound. IL-2 acts as a pleiotropic mediator within the immune system, having a variety of effects via specific cell surface receptors. The interaction of IL-2 with the IL-2 receptor induces proliferation and differentiation of a number of T lymphocyte subsets, and stimulates a cytokine cascade that includes various interleukins, interferons and tumour necrosis factors. Antitumour effects of IL-2 appear to be mediated by its effects on natural killer, lymphokine-activated killer (LAK) and other cytotoxic cells. In vivo and in vitro effects of IL-2 seem to be dependent to a large extent on the environment; many studies have reported conflicting results, perhaps due to diverse populations of effector cells, the availability of other cytokines that have synergistic or inhibitory influences, and the dosage regimens used. The recombinant products appear to be biologically indistinguishable from native IL-2 in vitro and in vivo; the former induce minor antibody formation but this does not appear to alter functional properties.

In patients with metastatic renal cell carcinoma, IL-2 therapy achieves average objective response rates of 20% (range 0 to 40%), with a complete response rate of about 5% (range 0 to 19%). Response duration varies considerably but can be durable (lasting for >12 months), with some patients remaining in complete response for >60 months. It is unclear at present whether higher dosage regimens improve clinical response, or whether combination therapy with other agents and/or adoptive therapy is beneficial. Survival duration may depend on the risk factors present, with poorer performance status and more than one site of metastases associated with shorter survival times. Patients with metastatic malignant melanoma receiving IL-2 as monotherapy show an average objective response rate of 13% (range 3 to 24%); however, objective response rate averages 30% (range 4 to 59%) when IL-2 is used in combination with other agents. Overall median survival appears to be about 10 months. Preliminary data indicate that IL-2 produces a lower response rate in patients with refractory colorectal carcinoma, ovarian cancer, bladder cancer, acute myeloid leukaemia or non-Hodgkin’s lymphoma. Adverse effects accompanying high dose, intravenous IL-2 therapy can be severe, with cardiovascular, pulmonary, haematological, hepatic, neurological, endocrine, renal and/or dermatological complications frequently requiring doses to be withheld. Typically, these effects resolve rapidly with cessation of IL-2 therapy, and may be reduced considerably with regional or subcutaneous administration.

In conclusion, IL-2 offers hope to some patients with renal cell carcinoma, malignant melanoma and other neoplastic disease, but appropriate patient selection and optimum dosage regimens