Submission from Jan Darby

Inquiry into availability of new, innovative and specialist cancer drugs in Australia

Purpose

To raise awareness of patients with desmoid tumours and their inability to access some drugs with known efficacy through the Pharmaceutical Benefits Scheme.

Background

Desmoid tumours (also called aggressive fibromatosis, deep musculoaponeurotic fibromatosis, and fibrosarcoma grade I of the desmoid type) are locally aggressive tumours with no known potential for metastasis. However, tumour invasion into vital structures and/or organs can result in substantial morbidity and may be fatal, especially in the case of intra-abdominal desmoids arising in patients with familial adenomatous polyposis (FAP). Desmoid tumours are responsible for 9 to 11 percent of deaths among patients with FAP.

Desmoid tumours are rare and estimated to occur in 2-4 people per million. They can develop at virtually any site in the body and affect all age groups, from babies and young children, through teens to young, middle-aged and older adults. Desmoids inside the abdomen can cause severe pain, rupture of intestines, compression of the kidneys or ureters or rectal bleeding. They can compress critical blood vessels such as the mesenteric vessels and the vena cava. Desmoid tumours may have multiple sites of origin on chest, arms or legs and can result in the amputation of limbs.

Because desmoid tumours lack the ability to metastasise, local control using surgery and radiation has traditionally been the mainstay of therapy. However, there is a significant risk of local recurrence, even after complete surgical resection. Estimations of recurrence vary, but are high (25 to 40 percent of patients up to 60 percent, depending on the study). Surgery may be difficult and even impossible for desmoids within the abdomen.

Radiation therapy is an effective option for many patients who cannot have surgery, or as an adjunct to surgery or chemotherapy. The duration of radiation treatment typically is 6 to 8 weeks. Radiographic evidence of tumour shrinkage may take months to years to

become apparent. Radiation therapy is often not considered an option in intra-abdominal tumours because of the size of the area needed to be irradiated and the risk of radiation damage to vital structures.

There is no single accepted medical treatment for desmoid tumours. Numerous reports of individual cases show shrinkage or stabilization of tumour size or at least improvement in symptoms after a very wide variety of treatments. A few chemotherapies commonly used include doxorubicin, Doxil, dacarbazine, methotrexate, vinorelbine and vinblastine. There have also been anecdotal reports of using sulindac (non-steroidal anti-inflammatory) or anti-hormonal agents such as tamoxifen.

New drugs

Tyrosine kinase inhibitors (such as Gleevec) have shown to be of benefit in some desmoid tumors. And recently there was remarkable activity noted in sorafenib (Nexavar). These newer agents are oral pills and are more tolerable than cytotoxic chemotherapies.
See http://www.ncbi.nlm.nih.gov/pubmed/21447727

Clin Cancer Res. 2011 Jun 15;17(12):4082-90. doi: 10.1158/1078-0432.CCR-10-3322. Epub 2011 Mar 29.

Activity of Sorafenib against desmoid tumor/deep fibromatosis.

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Abstract

BACKGROUND:

Desmoid tumors (deep fibromatoses) are clonal connective tissue malignancies that do not metastasize, but have a significant risk of local recurrence, and are associated with morbidity and occasionally mortality. Responses of desmoid patients to sorafenib on an expanded access program led us to review our experience.

METHODS:

After Institutional Review Board (IRB) approval, we reviewed data for 26 patients with desmoid tumors treated with sorafenib. Sorafenib was administered at 400 mg oral daily and adjusted for toxicity.

RESULTS:

Sorafenib was the first-line therapy in 11/26 patients and the remaining 15/26 had received a median of 2 prior lines of therapy. Twenty-three of 26 patients had shown evidence of progressive disease by imaging, whereas 3 patients had achieved maximum benefit or toxicity with chemotherapy. Sixteen of 22 (~70%) patients reported significant improvement of symptoms. At a median of 6 months (2-29) of treatment, the best response evaluation criteria in solid tumors (RECIST) 1.1 response included 6/24 (25%) patients with partial response (PR), 17/24 (70%) with stable disease, and 1 with progression and death. Twelve of 13 (92%) patients evaluated by MRI had > 30% decrease in T2 signal intensity, an indirect metric for increased fibrosis and loss of cellularity. Eighty percent of patients with radiological benefit had extra-abdominal desmoids.

DISCUSSION:

Sorafenib is active against desmoid tumors. A prospective, randomized clinical trial of sorafenib against other active agents is warranted.

Please note there is currently a trial recruiting patients titled 'Sorafenib tosylate in treating patients with desmoid tumors or aggressive fibromatosis':

SORAFENIB TOSYLATE IN TREATING PATIENTS WITH DESMOID TUMORS OR AGGRESSIVE FIBROMATOSIS

This study is currently recruiting participants.

Last Updated: November 2014

Sponsored by:	National Cancer Institute (NCI)
Information provided by:	Mrinal Gounder, MSKCC
Clinical Trials.gov Identifier:	NCT02066181
For detailed information click here:	http://clinicaltrials.gov/ct2/show/NCT02066181?term=desmoid+tumors&rank=3

Purpose: This randomized phase III trial compares the effects, good and/or bad, of sorafenib tosylate in treating patients with desmoid tumors or aggressive fibromatosis. Sorafenib tosylate may stop the growth of tumor cells by blocking some of the proteins needed for cell growth.

Argument

There are already numerous incidences where treatment of desmoids using sorafenib has been successful in the United States. One desmoid patient in Australia has undertaken a 2 year course of sorafenib with excellent results.

However, in Australia, sorafenib is only available through the Pharmaceutical Benefits Scheme for people with liver cancer. For others, the cost is $6,457.42 for 120 tablets

(1-2 months treatment for desmoid tumours, depending on the dose). Treatment can be from 1-2 years and therefore, well out of reach for the average patient.

The surgery, radiation and cytotoxic drug therapies often result in poor outcomes for desmoid tumour patients.

Recommendation

That consideration be given to funding sorafenib for desmoid tumour patients through the Pharmaceutical Benefits Scheme.

Although this would be a cost to the Australian Government, consideration of this funding needs to be made as, being a rare disease, there are very few patients (estimated to be fewer than 100 throughout Australia).

Not all patients would be candidates for, or would avail themselves of, sorafenib if given the opportunity.

For a comparatively small outlay, there could be the provision of hope and a massive reduction in pain, suffering, mobility issues, surgeries, radiotherapies and psychological trauma associated with being diagnosed with an incurable disease and having an unknown prognosis.

Background information taken from www.dtrf.org/index.php/about-br-desmoid-tumors/about-desmoid-tumors.html by

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