European Journal of Cancer (2015) 51, 2609–2614

Available at www.sciencedirect.com

ScienceDirect

journal homepage: www.ejcancer.com

Imatinib in advanced chordoma: A retrospective case series analysis

Nadia Hindi [a,*], Paolo G. Casali [a], Carlo Morosi [b], Antonella Messina [b], Elena Palassini [a], Silvana Pilotti [c], Elena Tamborini [c], Stefano Radaelli [d], Alessandro Gronchi [d], Silvia Stacchiotti [a]

[a] *Adult Mesenchymal Tumour and Rare Cancer Medical Oncology Unit, Cancer Medicine Department, Fondazione IRCCS Istituto Nazionale dei Tumori, Via G Venezian 1, 20133 Milan, Italy*
[b] *Department of Radiology, Fondazione IRCCS Istituto Nazionale dei Tumori, Via G Venezian 1, 20133 Milan, Italy*
[c] *Department of Pathology and Molecular Biology, Fondazione IRCCS Istituto Nazionale dei Tumori, Via G Venezian 1, 20133 Milan, Italy*
[d] *Department of Surgery, Fondazione IRCCS Istituto Nazionale dei Tumori, Via G Venezian 1, 20133 Milan, Italy*

Received 24 March 2015; received in revised form 9 May 2015; accepted 27 July 2015
Available online 14 August 2015

KEYWORDS
Chordoma
Imatinib
Sarcoma
Chemotherapy
Targeted therapy
Metastasis

Abstract ***Introduction:*** Imatinib showed activity in 50 chordoma patients treated within a Phase II study. In that study, 70% of patients remained with stable disease (SD), median progression free survival (PFS) was 9 months and median overall survival (OS) was 34 months. We now report on a retrospective series of PDGFB/PDGFRB positive advanced chordoma patients treated with imatinib as a single agent within a compassionate-use programme at Istituto Nazionale Tumori, Milan, Italy (INT) between August 2002 and November 2010, when the programme was closed.

Methods: 48 patients were consecutively treated with imatinib 800 mg/d. All patients had inoperable and progressive disease before starting imatinib. Demographics, treatment duration, toxicity and response rate by Response Evaluation Criteria in Solid Tumors (RECIST) were retrospectively recorded.

Results: The median duration of therapy was 7 months (1–46.5). No patient is on therapy at present. 46 patients were evaluable for response. No partial responses were detected. Best response was: stable disease 34 (74%), progressive disease 12 (26%). At a median follow-up of 24.5 months (0.5–117), median PFS was 9.9 months (95% confidence interval (CI) 6.7–13). Eight patients (16.5%) remained on therapy >18 months and 10 patients (21%)

Presented at Connective Tissue Oncology Society Annual Meeting 2014, Berlin, Abstract # 85.
The corresponding author has received a research grant from the Spanish Society of Medical Oncology (SEOM).
* *Corresponding author.*
E-mail address: nadiahindi83@gmail.com (N. Hindi).

http://dx.doi.org/10.1016/j.ejca.2015.07.038

remained progression-free >18 months. Median OS was 30 months (95% CI 20–40), with 24 (50%) patients dead at the time of the present analysis.

Conclusions: We confirm the activity of imatinib in locally advanced and metastatic chordoma, in terms of >70% tumour growth arrest in previously progressive patients. Median duration of response lasted almost 10 months, with >20% of patients progression-free at 18+ months.

1. Introduction

Chordoma is a rare primary bone tumour that arises from notochord remnants on axial bones (skull base and spine). Chordoma is usually a slow growing, locally aggressive disease, although up to 30% of patients can develop distant metastases. Surgery with wide margins is the mainstay of therapy in these patients, but more than 50% of them suffer from a local recurrence [1,2]. High-dose radiotherapy (RT) can be an option in the case of locally advanced disease [3,4], and as adjuvant therapy after a positive-margin surgery [5]. Cytotoxic chemotherapy is generally inactive in this tumour, and at present, no active drugs are approved for this indication. Imatinib had previously shown activity in chordoma. A multicentric Phase II trial with imatinib in patients with advanced disease showed only one partial response according to the Response Evaluation Criteria in Solid Tumors (RECIST) [6] but 70% of patients remained stable, with a median progression free survival (PFS) of 9 months [7].

Our institution previously reported on the outcome of 138 patients with primary, completely resected chordoma, observing that >50% of them died of disease [1]. Given this evidence and the previously reported data on the activity of imatinib, we decided to extend the use of imatinib within a compassionate-use programme that was opened after the closure of the Phase II trial, at Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy (INT) from August 2002 to November 2010.

Here we report on the retrospective series of advanced chordoma patients treated with imatinib within that programme.

2. Methods

2.1. Patients

This retrospective series includes 48 adult patients with progressive, locally advanced or metastatic chordoma consecutively treated with imatinib as single agent between August 2002 and November 2010 at INT. Performance Status (Eastern Cooperative Oncology Group) (ECOG) ⩽3 and adequate bone marrow and organ function were requested in all cases. Histologic diagnosis was confirmed by central review. Expression of PDGFB and/or PDGFRB was assessed in all patients by immunohistochemistry (IHC) (PDGFRB) and reverse transcriptase polymerase chain reaction (RT-PCR) from formalin fixed paraffin embedded (FFPE) samples (PDGFB). All patients provided a written informed consent to a non-conventional medical treatment, selected due to the lack of alternative effective drugs in the disease. Approval by the Institutional Review Board was provided.

2.2. Treatment

Patients received oral imatinib 800 mg/day, continuously, until progression or unacceptable toxicity. Treatment was temporarily withheld in case of grade ⩾3 toxicity according to the National Cancer Institute Common Toxicity Criteria (CTC), and restarted after recovery until grade <2.

2.3. Clinical and radiological assessments

Clinical examination, blood count and biochemistry were evaluated at the baseline and then monitored monthly during therapy. Toxicity was recorded. Baseline thoraco-abdominal computed tomography (CT) scan and magnetic resonance imaging (MR) of the primary tumour site documenting a RECIST disease progression in the previous 6 months were mandatory. CT/MR were repeated every 3 months. Some patients also performed at baseline [18F] fluorodeoxyglucose positron-emission tomography scan (PET) which was repeated every 3 months.

2.4. Efficacy assessment

Response was assessed according to RECIST (version 1.0) [6]. PET response was evaluated according to the European Organization for Research and Treatment of Cancer (EORTC) 1999 criteria [8]. Overall survival (OS) and progression free survival (PFS) were estimated by the Kaplan–Meier method. All patients receiving at least one dose of imatinib were included in the analysis. Patients were censored at the last contact. Death of any cause was considered therapy failure. Statistical analysis was performed with SPSS version 20.0.