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Dasatinib induced pleural effusions - Reply

Mohammad AJ Abdulla, Mohamed A Yassin

Hematology Section, National Center for Cancer Care and Research, Hamad Medical Corporation, (HMC), Doha, Qatar

Thanks for the reply with the title: "Dasatinib Induced Pleuro – Pericardial Effusion", we will discuss this issue in more details.

Dasatinib (Sprycel; Bristol-Myers Squibb, New York, NY) is a second-generation tyrosine-kinase inhibitor (TKI) approved for the first- and second-line treatment of chronic myeloid leukemia (CML) patients. It has been approved in the US and Europe since 2006. Dasatinib targets most imatinib-resistant BCR-ABL mutations (except the T315I and F317V mutants) by distinctly binding to active and inactive ABL-kinase. Kinase inhibition halts proliferation of leukemia cells. It also inhibits SRC family (including SRC, LKC, YES, FYN); c-KIT, EPHA2 and platelet derived growth factor receptor (PDGFRβ).

The current recommended starting doses of dasatinib are: 100 mg daily for CML in chronic phase, and 140 mg daily for CML in accelerated or blast phase. With these doses, toxicity is not uncommon, with hematologic toxicity being the most common.

It should be kept in mind that dasatinib is metabolized by CYP3A4 system, so if administered concomitantly with strong CYP3A4 inhibitors and grapefruit juice, toxicity will increase, so the dose should be reduced. Conversely, if administered concomitantly with strong CYP3A4 inducers and St John's wort, the dose should be increased with close monitoring.

Of the Bcr-Abl TKIs, dasatinib has been associated with the highest frequency of pulmonary side effects. During treatment with dasatinib, pleural, pulmonary vascular, and lung parenchymal abnormalities can develop separately or simultaneously. Between 10 and 35 percent of patients treated with dasatinib in clinical trials developed pleural effusions, most often exudative and lymphocyte predominant (1-3). Dasatinib-induced effusions may be a result of PDGFR inhibition, but some clinicians suspect that it is a result of lymphatic drainage abnormalities and microvasculopathy associated with a protein leak (2).

Optimal treatment of dasatinib-related pleural effusions, when they occur, is not known. In case series, treatment has included systemic glucocorticoids, diuretics, thoracentesis, and dasatinib interruption or discontinuation (1, 3). Rarely, pleurodesis has been used (4). Combinations of the above therapies have also been employed.

It has been shown in small studies that lower doses of dasatinib are better tolerated and associated with less side effects, while efficacy is not affected [100 mg daily vs higher dose (5), 50 mg daily vs higher dose (6)]. We applied this in the case we previously reported with excellent results (7).

In conclusion, pleural effusions occur in up to one-third of patients treated with dasatinib at the current recommended doses, with hematologic toxicity being much more common, so maybe in the future, with larger studies, recommended doses might be reduced.

Conflict of interest: Each author declares that he has no commercial associations (e.g. consultancies, stock ownership, equity interest, patent/licensing arrangement etc.) that might pose a conflict of interest in connection with the submitted article

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Correspondence:
Mohamed A Yassin
Hematology Section, National Center for Cancer Care and Research, Hamad Medical Corporation, (HMC), Doha, Qatar
E-mail: yassinmoha@gmail.com