Poster
P075

Ponatinib Facilitates Treatment-free Remission by Inducing Deep Molecular Responses

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Multiple trials now demonstrate the potential for success and the safety of an attempt at treatment-free remission (TFR) in patients with sustained deep molecular response to tyrosine kinase inhibitors (TKIs) [1,2,3]. We describe two patients who remain in treatment-free remission after achieving undetectable BCR-ABL with ponatinib on the phase II PACE trial, despite being multiply resistant/intolerant to other agents or carrying the T315I mutation.

PATIENT 1

Previously was intolerant of imatinib and nilotinib due to Grade 3 rash and dasatinib and interferon alpha-2a due to grade 3 liver enzyme abnormalities. On each occasion the patient had toxicity from a TKI, he was rechallenged and repeatedly had toxicity. He had a suboptimal response to his initial TKI therapy (BCRABL >10% at 15mo).

Pre-trial co-morbidities included diet-controlled diabetes, ischaemic heart disease (mild angina 20 years earlier with minor disease on angiogram), hypertension, hypercholesterolaemia and gastro-oesophageal reflux.

He was enrolled on the PACE study 27 months post-diagnosis, age 63. His ponatinib dose was reduced from 45mg/d to 30mg/d within the first two weeks due to an early grade 3 lipase elevation. He subsequently had a myocardial infarction requiring coronary artery bypass grafts at 1 year and then an 80-99% incidentally discovered carotid stenosis requiring endarterectomy at 26mo. At 27mo ponatinib was reduced to 15mg/d due to weight loss of 20%, anorexia, abdominal pain and grade 2 alkaline phosphatase elevation. At 29mo a colonoscopy showed an ulcerated, strictured ascending colon with non-specific findings on biopsy. His ponatinib was withheld and restarted after a month. At 52mo he developed recurrent, presumed ischaemic, colitis.

His BCR-ABL fell to 0.15% at 3 months (Molecular MD laboratories), 0.0014% at 6 months and was undetectable at 8 months and remains so. At the time of his last episode of colitis, his BCR-ABL had been undetectable for 44 months and hence a decision to attempt TFR was made. He remains in TFR 12 months post-cessation.

PATIENT 2

Achieved a suboptimal response to front-line imatinib with a BCR-ABL level of 2.14% two years after diagnosis. He was switched to dasatinib but had persistently high level and was found to carry the T315I mutation 5 years after diagnosis when his BCR-ABL level rose from 1.67% to 9.5%.

Pre-trial co-morbidities included diet-controlled diabetes and gout.
He was enrolled on the PACE study 66 months post-diagnosis, age 64. His ponatinib dose was also reduced from 45mg/d to 30mg/d within 2 weeks due to grade 3 lipase elevation and grade 3 hyperglycaemia, requiring insulin. His course was complicated by a sub-arachnoid haemorrhage at 4 months and cystoid macular oedema at 10 months. At 23mo he developed claudication and required stenting to a popliteal artery stenosis. This was complicated by restenosis requiring stent revision and bilateral embolic strokes presumed secondary to atheromatous disease in is proximal aorta. His ponatinib was reduced to 15mg/d. At 37mo he required multiple coronary stents for angina.

His BCR-ABL fell to 0.025% at 3 months, and was undetectable by 9 months and remains so. At the time of review after his last event, his BCR-ABL had been undetectable for 30 months and hence a decision to attempt TFR was made. He remains in TFR 18 months post-cessation.

CONCLUSION

This series adds to the one prior case report of ponatinib facilitating treatment-free remission [4] and these remissions are notable because they occur in patients not considered for other TFR studies because of refractoriness to other agents or known T315I mutations. They illustrate the potency of ponatinib and provide an alternative avenue to dose reduction to reduce the risk of vascular events in ponatinib-treated patients.

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