NEW DRUGS

Aust Prescr 2018;41:94
https://doi.org/10.18773/austprescr.2018.025
First published 15 May 2018

Sonidegib

Approved indication: basal cell carcinoma

Odomzo (Sun)
200 mg capsules

Basal cell carcinoma is a common skin cancer. Usually it is slow growing and local treatment is effective. Sometimes the cancer becomes locally advanced and can metastasise. Sonidegib can be considered in these cases if patients cannot be managed with surgery or radiotherapy.

The development of basal cell carcinoma is thought to involve the hedgehog gene. Normally this has a role in regulating cell development, however abnormal activation of this signalling pathway can lead to the proliferation of cancer cells. Sonidegib is an antagonist of the hedgehog pathway to inhibit further signalling.

The drug is poorly absorbed and the capsules should be taken on an empty stomach. It takes about four months to reach a steady-state concentration. The concentration of sonidegib is higher in skin than in plasma. Sonidegib is partly metabolised by cytochrome P450 (CYP) 3A4 with most of the drug and its metabolites being excreted in the faeces. Strong inhibitors of CYP3A4, such as itraconazole and ritonavir, should not be given with sonidegib. Co-administration with strong inducers, such as carbamazepine and rifampicin, should also be avoided. No dose adjustment is recommended in hepatic or renal impairment.

The Australian approval of sonidegib appears to have been based mainly on one uncontrolled phase II trial. It randomised 79 patients to take sonidegib 200 mg and 151 to take 800 mg once daily. There were 194 patients with locally advanced disease and 36 with metastases. The Response Criteria In Solid Tumours (RECIST) were used to assess the effect of treatment. After a median follow-up of almost 14 months, 36% of the patients taking 200 mg and 34% of those taking 800 mg had responded. Apart from two patients with complete responses, these were all partial responses.[1]

A longer term analysis of the results (30 months after the last patient was randomised) reported higher response rates. For patients with locally advanced basal cell carcinoma, the response rate was 56.1% with 200 mg and 45.3% with 800 mg. The corresponding figures for metastatic disease were 7.7% and 17.4%.[2]

At the time of the 30-month analysis, 93% of the patients had stopped sonidegib. This was mainly because of adverse events, particularly with the 800 mg dose. The common adverse events were muscle spasm, alopecia, dysgeusia, nausea, decreased appetite and fatigue. Musculoskeletal problems are a class effect of hedgehog inhibitors.

In view of the risk of rhabdomyolysis, creatine kinase concentrations should be checked. The risk is likely to be increased if the patient is also taking a statin. Treatment may need to be stopped if creatine kinase is greatly elevated. Sonidegib is contraindicated in pregnancy and men should use condoms to avoid exposing their partners to the drug. Patients should not donate blood for at least 20 months after stopping sonidegib.

The recommended dose for clinical use is 200 mg daily as 800 mg is not more efficacious and causes more adverse effects. As basal cell carcinoma is slow growing, even after 30 months the median overall survival had not been reached. The estimated survival rate at two years in patients taking 200 mg was 93.2% for advanced disease and 69.3% for those with metastases, but there was no comparison with current managment.[2] Few patients had a complete response which suggests that more than the hedgehog pathway is involved in tumour growth. As some tumours may be resistant to treatment, the optimum use of sonidegib will require further investigation.

T T manufacturer provided additional useful information

REFERENCES

1. Migden MR, Guminski A, Gutzmer R, Dirix L, Lewis KD, Combemale P, et al. Treatment with two different doses of sonidegib in patients with locally advanced or metastatic basal cell carcinoma (BOLT): a multicentre, randomised, double-blind phase 2 trial. Lancet Oncol 2015;16:716-28. https://doi.org/10.1016/S1470-2045(15)70100-2
2. Lear JT, Migden MR, Lewis KD, Chang ALS, Guminski A, Gutzmer R, et al. Long-term efficacy and safety of sonidegib in patients with locally advanced and metastatic basal cell carcinoma: 30-month analysis of the randomized phase 2 BOLT study. J Eur Acad Dermatol Venereol 2018;32:372-81. https://doi.org/10.1111/jdv.14542

The Transparency Score is explained in New drugs: transparency, Vol 37 No 1, Aust Prescr 2014;37:27.

At the time the comment was prepared, information about this drug was available on the websites of the Food and Drug Administration in the USA, the European Medicines Agency.

SUBSCRIPTIONS

A:

ANSWERS TO SELF-TEST QUESTIONS

1 True
2 True
3 False
4 False

EDITORIAL OFFICE

For general correspondence such as Letters to the Editor, contact the Editor.

Postal The Editor
Australian Prescriber
PO Box 104
DEAKIN WEST 2600

Telephone (02) 6202 3100

Fax (02) 6282 6855

Email info@australianprescriber.com

Website nps.org.au/australianprescriber

Twitter @AustPrescriber

SUBSCRIPTIONS

Australian Prescriber is published every two months online. All content is accessible free of charge in full text at nps.org.au/australianprescriber. New drugs are published between issues as they become available.

An email alert can be sent to you when *Australian Prescriber* publishes new material. Subscribe or update your details at nps.org.au/australianprescriber

For back issues, and copies of the Anaphylaxis wallchart and Switching-antidepressants poster, email info@australianprescriber.com