“I’m J.D. and I need your support.”

We invite you to join us at the EAHP GSK Symposium 'My role as a pharmacist in managing mRCC* and aSTS* patients on Votrient® (pazopanib)'

Wednesday March 13th 2013, 16h15-17h45 in Salle Maillot, Le Palais des Congrès de Paris, France

Speakers:

Dr Christophe Bardin (France)
Oncology Pharmacist, Hôpital Cochin AH-HP, Paris

Jürgen Barth (Germany)
Oncology Pharmacist, Justus-Liebig University, Giessen

Dr Alexandre Chan (Singapore)
Associate Consultant Oncology Pharmacist, National Cancer Centre, Singapore

Format:

1. Review two oncology patient case studies

2. Discuss practical management tips

3. Share solutions with speakers

Objectives:

1. Identify the key decision points undertaken by pharmacists across the patient journey

2. Provide practical advice on the role of clinical pharmacists in the management of mRCC* and aSTS* patients on Votrient®

3. Share collective knowledge and expertise

* mRCC: metastatic Renal Cell Carcinoma * aSTS: advanced Soft Tissue Sarcoma

gsk GlaxoSmithKline Oncology

Prescribing Information (Please refer to full SmPC before prescribing)

General information

Votrient® (pazopanib) 200mg and 400mg film-coated tablets. Each tablet contains pazopanib hydrochloride, equivalent to 200mg and 400mg of pazopanib, respectively. **Indications** In adult patients for: first-line treatment of advanced renal cell carcinoma (RCC) and those with prior cytokine therapy; treatment of selective subtypes of advanced soft tissue sarcoma (STS) who have received prior chemotherapy for metastatic disease or who have progressed ≤12 months after (neo) adjuvant therapy. Efficacy and safety only established in certain histological tumour subtypes. Excluded subtypes: adipocytic sarcoma; GIST; all rhabdomyosarcoma that are not alveolar or pleomorphic; chondrosarcoma; osteosarcoma; Ewing tumours/PNET; dermatofibromatosis sarcoma protuberans; inflammatory myofibroblastic sarcoma; malignant mesothelioma; mixed mesodermal tumours of the uterus. **Dosage and administration** (STS and RCC) Only to be initiated by physician experienced in use of anti-cancer agents. 800mg once daily. Take without food (≥1 hour before or ≥2 hours after a meal). Take tablets whole; do not break or crush. Dose modification: In 200mg steps based on individual tolerability to manage ADRs. Not to exceed 800mg. Renal impairment: No dose adjustment required in patients with CrCl >30ml/min. Caution advised in patients with CrCl <30ml/min. Hepatic impairment: Severe hepatic impairment - Not recommended. Undertake with caution and close monitoring in mild/moderate impairment. Mild impairment - 800mg once daily; Moderate impairment - 200mg once daily. Elderly: Limited data in patients ≥ 65 yrs. Paediatrics: Not to be used in children <2 yrs. Safety & efficacy not established in children 2-18 yrs; no data available. **Contra-indications** Hypersensitivity to active substance or excipients. **Special Warnings and Precautions** Hepatic effects: Hepatic failure reported during pazopanib use; increases in serum transaminases (ALT, AST) and bilirubin also observed. Monitor liver function before initiation of treatment and ≥once every 4 weeks for first 4 months, and periodically thereafter. If transaminases ≤8xULN, continue pazopanib with weekly monitoring until they return to ≤Grade 1. If transaminases >8xULN, interrupt pazopanib until they return to ≤Grade 1. If transaminases >3xULN occur following re-introduction, discontinue pazopanib. If transaminases >3xULN occur concurrently with bilirubin >2xULN, perform bilirubin fractionation. If direct (conjugated) bilirubin is >35% of total, discontinue pazopanib. Concomitant use of pazopanib and simvastatin increases risk of ALT elevations: undertake with caution and close monitoring. Hypertension: Events of hypertension, including hypertensive crisis, have occurred in pazopanib studies. Control BP prior to initiating pazopanib. Monitor for hypertension early (≤1 week after starting treatment) and frequently thereafter. Manage elevated BP with anti-hypertensive therapy and pazopanib dose modification. Discontinue pazopanib if BP is persistently elevated (140/90 mmHg) or if arterial hypertension is severe and persists despite anti-hypertensive therapy and dose reduction. Cardiac dysfunction/heart failure: Consider risks/benefits of pazopanib in patients with pre-existing cardiac dysfunction. Safety and pharmacokinetics of pazopanib not studied in patients with moderate to severe heart failure or those with below normal LVEF. Events of cardiac dysfunction (e.g. CHF and LVEF decline) have occurred in pazopanib trials. Monitor patients for signs and symptoms of CHF. Baseline and periodic LVEF evaluation recommended. QT prolongation and Torsade de Pointes: Use with caution in patients (i) with history of QT interval prolongation, (ii) taking antiarrythmics or other medications that may prolong QT interval or (iii) with relevant pre-existing cardiac disease. Baseline and periodic ECGs, and maintenance of electrolytes within normal range recommended. Arterial thrombotic events: Use with caution in patients at increased risk for these events. Base treatment decision on individual patient's benefit/risk assessment. Venous thromboembolic events (VTEs): VTEs including venous thrombosis and fatal pulmonary embolus have occurred in pazopanib trials. Haemorrhagic events: Not recommended in patients with history of haemoptysis, cerebral, or significant GI haemorrhage in past 6 months. Use with caution in patients with significant risk of haemorrhage. GI perforations and fistula: Use with caution in patients at risk for GI perforation or fistula. Wound healing: Stop treatment ≥7 days prior to surgery. Resume after surgery based on clinical judgement of adequate wound healing. Discontinue pazopanib in patients with wound dehiscence. Hypothyroidism: Baseline measurement of thyroid function recommended prior to start of pazopanib treatment; monitor periodically during treatment. Monitor patients for signs and symptoms of thyroid dysfunction and manage as per standard medical practice. Proteinuria: Baseline and periodic urinalysis recommended. Monitor patients for worsening proteinuria. Discontinue pazopanib if Grade 4 proteinuria develops. Pneumothorax: Observe patients closely for signs and symptoms of pneumothorax. Infections: Cases of serious infection (with/without neutropenia) reported. **Interactions** Avoid concomitant use with strong inhibitors of CYP3A4, p-glycoprotein (P-gp) or breast cancer resistance protein (BCRP) and CYP3A4 inducers. Hyperglycaemia observed during concomitant administration with ketoconazole. Undertake concomitant administration with uridine diphosphate glucuronosyl transferase 1A1 (UGT1A1) substrates and simvastatin (and other statins) with caution. Avoid grapefruit juice during pazopanib treatment. **Pregnancy and lactation** No adequate data on use in pregnant women. Not to be used unless clearly necessary; appropriate contraception advised. Not known whether pazopanib excreted in human milk; breastfeeding should be discontinued. Animal studies indicate fertility may be affected. **Effects on ability to drive and use machines** No studies conducted. Avoid driving or using machines if affected. **Undesirable effects** Most important serious ADRs associated with pazopanib in RCC and STS clinical studies were: TIA, ischaemic stroke, myocardial ischaemia, myocardial and cerebral infarction, cardiac dysfunction, GI perforation and fistula, QT prolongation, pulmonary/GI/cerebral haemorrhage. All events occurred in <1% of patients. Other important serious ADRs in STS trials included VTEs, LV dysfunction and pneumothorax. Fatal events possibly related to pazopanib included: GI haemorrhage, pulmonary haemorrhage/haemoptysis, abnormal hepatic function, intestinal perforation, ischaemic stroke. **Overdose** No specific antidote. Treatment should consist of general supportive measures. **Treatment-related events with pazopanib in advanced RCC patients reported with following frequencies:** Very common: decreased appetite; dysgeusia; hypertension; diarrhoea, nausea, vomiting, abdominal pain; hair colour changes; fatigue; increased ALT and AST. Common: thrombocytopenia, neutropenia, leucopenia; hypothyroidism; headache, dizziness, lethargy, paraesthesia; hot flush; epistaxis, dysphonia; dyspepsia, stomatitis, flatulence, abdominal distension; abnormal hepatic function, hyperbilirubinaemia; rash, alopecia, PPE, skin hypo/de-pigmentation, erythema, pruritus, dry skin, hyperhidrosis; myalgia, muscle spasms; proteinuria; asthenia, mucosal inflammation, oedema, chest pain; decreased weight /WBC, increased creatinine / bilirubin / lipase / BP / TSH / GGT. Uncommon events include: hypophosphataemia; hypomagnesaemia; peripheral sensory neuropathy; hypoaesthesia; eyelash discolouration; CVA, myocardial infarction, bradycardia; flushing, hypertensive crisis; mouth ulceration, frequent bowel movements; pancreatitis, peritonitis; hepatotoxicity, hepatic failure, hepatitis; jaundice; photosensitivity reaction, skin exfoliation; menorrhagia, metrorrhagia, retroperitoneal / urinary tract / vaginal haemorrhage; mucous membrane disorder; increased blood urea / amylase, decreased blood glucose, abnormal thyroid function test; infections (with / without neutropenia). **Treatment-related events with pazopanib in advanced STS patients reported with following frequencies:** Very common: tumour pain; leucopenia, thrombocytopenia, neutropenia; decreased appetite, hyperalbuminaemia; dysgeusia, headache; hypertension; diarrhoea, nausea, vomiting, abdominal pain, stomatitis; hair colour change, skin hypopigmentation, exfoliative rash; fatigue; weight decreased; Common: gingival infection; hypothyroidism; dehydration; insomnia, peripheral sensory neuropathy, dizziness;vision blurred; cardiac / LV dysfunction, bradycardia; VTE, hot flush, flushing; epistaxis, dysphonia, dyspnoea, cough, pneumothorax, hiccups, pulmonary haemorrhage; abdominal distension, dry mouth, dyspepsia, mouth haemorrhage, flatulence, anal haemorrhage; alopecia, skin/nail disorder, dry skin, hyperhydrosis, pruritus, erythema; musculoskeletal pain, myalgia, muscle spasms; oedema, chest pain, chills; abnormal ENT exam, increased ALT / AST / GGT, abnormal blood cholesterol. Uncommon events include: hypomagnesaemia; somnolence, paraesthesia, cerebral infarction; myocardial infarction; haemorrhage; oropharyngeal pain, bronchial haemorrhage, rhinorrhoea, haemoptysis; peritonitis, enterocutaneous fistula, ileal perforation, gastric / rectal / oesophageal / retroperitoneal / vaginal haemorrhage, melaena; abnormal hepatic function; skin ulcer, rash, photosensitivity, PPE; proteinuria; menorrhagia; arthralgia; mucosal inflammation, asthenia; increased bilirubin, decreased platelet count, QT prolonged. **Marketing authorisation (MA) nos.** EU / 1 / 10 / 628 / 001-4. **MA holder** Glaxo Group Limited, Berkeley Avenue, Greenford, Middlesex UB6 0NN. **Legal category** POM.ONCE/PAZ/0102/12 January 2013.

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GSK has been involved in selecting the faculty and in the creation of the agenda and content