Seagen Breakfast Symposium

Extending overall survival in HER2-positive advanced breast cancer with TUKYSA®▼ (tucatinib) in combination with trastuzumab and capecitabine: Clinical evidence and case-based guidance

Friday 17 June 2022, 08:00–08:45

Meeting Room 1A, Level 3 I Belfast International Convention Centre (ICC)

Time	Topic	Speaker
08:00	Welcome and introduction	Dr Alicia Okines (Chair)
08:05	TUKYSA in HER2-positive locally advanced or metastatic breast cancer	Dr Mark Verrill
08:15	Example cases of patient management	Prof. Dr Christian Jackisch
08:25	MBC landscape: Panel discussion	All faculty
08:40	Closing remarks	Dr Alicia Okines

This is a promotional symposium for UK Healthcare Professionals organised by Seagen UK Ltd.

PRESCRIBING INFORMATION

TUKYSA® ▼ (tucatinib) 50 mg and 150 mg film-coated tablets.

This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions via the Yellow Card Scheme at: **www.mhra.gov.uk/yellowcard**. Adverse events should also be reported to Seagen on **0330 818 0490** or email **medinfoEU@seagen.com**

Please refer to the Summary of Product Characteristics (SmPC) for the full Prescribing Information.
Presentation: Film-coated tablets each containing 50 mg or 150 mg of tucatinib.
Indication: TUKYSA is indicated in combination with trastuzumab and capecitabine for the treatment of adult patients with HER2 positive locally advanced or metastatic breast cancer who have received at least 2 prior anti HER2 treatment regimens.
Dosage and Administration: Treatment should be initiated and supervised by a physician experienced in the administration of anti–cancer medicinal products. The recommended dose is 300 mg tucatinib orally twice daily continuously in combination with trastuzumab (given intravenously as an initial 8 mg/kg dose followed by 6 mg/kg IV every 21 days, or subcutaneously at 600 mg every 21 days) and capecitabine (1000 mg/m2 orally twice daily on days 1 to 14 every 21 days). Refer to the SmPC for co-administered trastuzumab and capecitabine for additional information. The treatment components can be administered in any order. Treatment with TUKYSA should be continued until disease progression or unacceptable toxicity. *Missed dose:* the patient should take their next dose at the regularly scheduled time. For recommended dose reductions or modifications in case of adverse reactions, please refer to the TUKYSA SmPC. Concomitant use with strong CYP2C8 inhibitors should be avoided. *Elderly:* No dose adjustment is required in patients aged ≥ 65 years. Tucatinib has not been investigated in patients above the age of 80 years. *Renal impairment:* no dose adjustment is required. *Hepatic impairment:* no dose adjustment is required in patients with mild or moderate hepatic impairment. For patients with severe hepatic impairment (Child-Pugh C), a reduced starting dose of 200 mg orally twice daily is recommended. *Paediatric population:* the safety and efficacy of TUKYSA in paediatric patients have not been established.
Contraindications: Hypersensitivity to the active substance or to any of the excipients.
Warnings and Precautions: Increased ALT, AST, and bilirubin have been reported during treatment with tucatinib. ALT, AST, and bilirubin should be monitored every three weeks or as clinically indicated. Based on the severity of the adverse reaction, treatment with tucatinib should be interrupted, then dose reduced or permanently discontinued. Increase in serum creatinine (30% mean increase) has been observed due to inhibition of renal tubular transport of creatinine without affecting glomerular function. Diarrhoea, including severe events such as dehydration, hypotension, acute kidney injury and death, has been reported during treatment with tucatinib. If diarrhoea occurs, antidiarrheals should be administered as clinically indicated. For Grade ≥3 diarrhoea, treatment with tucatinib should be interrupted, then dose reduced or permanently discontinued.
Interactions: Tucatinib is primarily metabolised by CYP2C8. Tucatinib is a metabolism-based inactivator of CYP3A and inhibits renal transporters of metformin and creatinine. Tucatinib is a substrate of P-gp. *CYP3A/CYP2C8 inducers:* Concomitant use of tucatinib with a strong CYP3A or moderate CYP2C8 inducer decreased tucatinib concentrations. Co-administration of tucatinib with strong CYP3A or moderate CYP2C8 inducers such as rifampicin, phenytoin, St. John's wort, or carbamazepine should be avoided as this may result in decreased activity of tucatinib. *CYP2C8 inhibitors:* Concomitant use of tucatinib with a strong CYP2C8 inhibitor increased tucatinib concentrations, which may increase the risk of tucatinib toxicity. Co-administration of tucatinib with strong CYP2C8 inhibitors such as gemfibrozil should be avoided as this may result in increased risk of tucatinib toxicity. Monitoring for tucatinib toxicity should be increased with moderate CYP2C8 inhibitors. *CYP3A inhibitors:* Co-administration of a single dose of 300 mg tucatinib with itraconazole (a strong CYP3A inhibitor) has resulted in an increase in tucatinib concentrations. No dose adjustment is required. *CYP3A substrates:* Tucatinib is a strong CYP3A inhibitor and has the potential to interact with medicinal products that are metabolised by CYP3A, which may lead to increased plasma concentrations of the other product. Concomitant use of tucatinib with CYP3A substrates (see SmPC for examples), when minimal concentration changes may lead to serious or life-threatening toxicities, should be avoided. If concomitant use is unavoidable, the CYP3A substrate dosage should be decreased in accordance with the concomitant medicinal product's SmPC. *P-gp substrates:* Concomitant use of tucatinib with a P-gp substrate may increase the plasma concentrations of the P-gp substrate, which may increase the toxicity associated with the P-gp substrate. Dose reduction of P-gp substrates (including sensitive intestinal substrate such as dabigatran) should be considered in accordance with the concomitant medicine's SmPC and P-gp substrates should be administered with caution when minimal concentration changes may lead to serious or life-threatening toxicities. *CYP2C8 substrates:* Coadministration of tucatinib with repaglinide (a CYP2C8 substrate) has resulted in an increase in repaglinide concentrations. No dose adjustment is required. *MATE1/2K substrates:* Co-administration of tucatinib with metformin (a MATE1/2-K substrate) has resulted in an increase in metformin concentrations. Tucatinib reduced the renal clearance of metformin without any effect on glomerular filtration rate (GFR). No dose adjustment is required.
Fertility, pregnancy and lactation: Tucatinib may cause harmful pharmacological effects when administered to women during pregnancy and/or on the foetus/newborn child. Women of childbearing potential should be advised to avoid becoming pregnant and to use effective contraception during and up to at least 1 week after treatment. Male patients with female partners of childbearing potential should also be advised to use effective contraception during and up to at least 1 week after treatment. It is unknown whether tucatinib/metabolites are excreted in human milk. Breast feeding should be discontinued during and up to 1 week after treatment. Tucatinib may impair fertility in females of reproductive potential.
Undesirable effects: epistaxis, diarrhoea, nausea, vomiting, stomatitis, rash, arthralgia, AST increase, ALT increase, blood bilirubin increased, and weight decrease were observed during treatment (*very common, ≥1/10*). Consult the SmPC for a full description of adverse reactions.
Overdose: There is no specific antidote, and the benefit of haemodialysis in the treatment of tucatinib overdose is unknown. In the event of an overdose, treatment with tucatinib should be withheld and general supportive measures should be applied.
Price: TUKYSA 50 mg film-coated tablets, carton of 88 tablets: £1,968.42
TUKYSA 150 mg film-coated tablets, carton of 84 tablets: £5,636.84
Legal category: POM
Marketing authorisation number: *Great Britain:* PLGB 34503/0001 (50 mg), PLGB 34503/0002 (150 mg);*Northern Ireland:* EU/1/20/1526/001 (50 mg), EU/1/20/1526/002 (150 mg)
Marketing authorisation holder: *Great Britain:* Seagen U.K. Ltd, The Charter Building, Charter Place, Uxbridge, UB8 1JG, UK; *Northern Ireland:* Seagen B.V., Evert van de Beekstraat 1-104, 1118CL Schiphol, The Netherlands
Date of preparation: December 2021
UK-TUP-21-154-MT

Check appropriate TUKYSA Summary of Product Characteristics for further information.

TUKYSA® tucatinib 50 mg | 150 mg tablets

Date of Preparation: June 2022 Job code: UK-TUP-22-203-MT