

Histopathological evaluation revealed that one of the patients had a non-germ cell tumor, a Sertoli cell tumor, while others had mixed germ cell tumors. Half of them had only a single right frontoparietal lesion (21 mm) or right occipital (42 mm), both were heterogeneous in T1WI and T2WI, and with intense and heterogeneous enhancement with gadolinium. The other two patients had multiple lesions. One of them had left frontoparietal (2.2 mm, hyperintense in T1) and right occipital (1.8 mm, hypointense in T1) lesions, both heterogeneous and predominantly hypointense in T2 and T1WI with no enhancement. The other had right temporal (5 mm) and left occipital (11 mm) lesions, both isointense in T1WI and T2WI with intense and homogeneous enhancement. There was no diffusion restriction in all three cases and all four cases were hypointense in T2\*.

**Conclusion:** Although the imaging features of brain metastases differ in some aspects, they all have a hemorrhagic component and a very low survival rate after diagnosis.

## References

- Huyghe E, Matsuda T, Thonneay P. Increasing incidence of testicular cancer worldwide: a review. *J Urol.* 2003;170:5–11.
- Sesterhenn IA, Chevillat J, Woodward PJ, et al. Sex cord/gonadal stromal tumours. In: Eble JN, Sauter G, Epstein JI, Sesterhenn IA, editors. *Pathology and genetics of tumours of the urinary system and male genital organs.* Lyon, France: IARC Press; 2004. p. 250–5.
- Raj S, Parkinson C, Williams M, Mazhar D. Management of brain metastases from germ cell tumors: do we know what we are doing? *Future Oncol.* 2008;4:1–4.
- Raina V, Singh SP, Kamble N, et al. Brain metastasis as the site of relapse in germ cell tumor of testis. *Cancer.* 1993;72:2182–5.
- Bower M, Newlands ES, Holden L, Rustin GJ, Begent RH. Treatment of men with metastatic non-seminomatous germ cell tumours with cyclical POMB/ACE chemotherapy. *Ann Oncol.* 1997;8:477–83.
- Bokemeyer C, Nowak P, Haupt A, et al. Treatment of brain metastases in patients with testicular cancer. *J Clin Oncol.* 1997;15:1449–54.
- Fossa SD, Bokemeyer C, Gerl A, et al. Treatment outcome of patients with brain metastases from malignant germ cell tumors. *Cancer.* 1999;85:988–97.
- Williams SD, Einhorn LH. Brain metastases in disseminated germinal neoplasms: incidence and clinical course. *Cancer.* 1979;44:1514–6.
- Kaye SB, Bagshawe KD, McElwain TJ, Peckham MJ. Brain metastases in malignant teratoma: a review of four years' experience and an assessment of the role of tumour markers. *Br J Cancer.* 1979;39:217–23.

<http://dx.doi.org/10.1016/j.pbj.2017.07.113>

## PS196

### Synthesis and tumor cell growth inhibitory effects of the marine product analogues of fiscalin B

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**Aim:** The aim of this work was to synthesize fiscalin B, to pursue the development of a library of derivatives and to investigate the derivatives for their potential antitumor activity.

**Introduction:** Marine organisms provided numerous novel compounds with sensational multiple pharmacological properties. The necessity of novel therapeutics has gain more importance especially because of the resistance associated to the current therapeutics and the inexistent treatments for incurable diseases. Fiscalin B is a fungal metabolite with a pyrazino[2,1-b]quinazoline-3,6-dione system reported to have significant biological activities.

**Methods:** Two methods were studied for synthesis – double cyclization and microwave assisted procedures. First method started with coupling reactions to form tripeptide of tryptophan methyl ester linked to N-Fmoc-valine via anthranilic acid. Then, the dehydrative cyclization was performed using formamide to form the intermediate oxazine. The coupling reaction to form the fiscalin B were achieved after deprotection.<sup>1</sup> The second method is the coupling of anthranilic acid with N-Boc-valine to form Boc-protected benzoxazin-4-one by thermal heating conditions. Then, the addition of tryptophan methyl ester hydrochloride led to 4-quinazoline-3,6-dione scaffold by microwave irradiation.<sup>2</sup> The cell growth inhibitory effect was investigated by the Sulforhodamine B assay.

**Results:** The use of amino acids with different configurations and different side chains or even the derivatization of the existing functional groups were enable the application of this synthetic methodology for a library of fiscalin B analogues. The formation yields of fiscalin B analogues were low, ranging from 3 to 16%. Eight derivatives were tested on non-small cell lung cancer (H460), colon adenocarcinoma (HCT15) and breast cancer (MCF7) human cell lines and showed moderate cytotoxic effects, with GI50 concentrations ranging from 30 to 80 µM.

**Conclusion:** Significant differences were obtained between enantiomeric pairs.

**Acknowledgements:** To national funds provided by FCT, ERDF, and COMPETE under the projects PEst-C/MAR/LA0015/2013, QOPNA (FCT UID/QUI/00062/2013), PTDC/MAR-BIO/4694/2014 (POCI-01-0145-FEDER-016790), PTDC/AAG-TEC/0739/2014 (POCI-01-0145-FEDER-016793), and INNOVMAR, reference NORTE-01-0145-FEDER-000035, Research Line NOVELMAR and grant reference NOVELMAR/BPD\_2/2016-019. To University of Aveiro and FCT/MEC for the financial support to the QOPNA research project (UID/QUI/00062/2013) financed by national funds and co-financed by FEDER under the PT2020, and to the Portuguese NMR Network. S.L. thanks Erasmus Mundus Action 2 (LOTUS+, LP15DF0205) for full PhD scholarship.

## References

- Wang H, Ganesan A. Total synthesis of the fumiquinazoline alkaloids: solution-phase studies. *J Organ Chem.* 2000;65:1022–30.
- Liu JF, Ye P, Zhang B, Bi G, Sargent K, Yu L, et al. Three-component one-pot total syntheses of gyantrypine, fumiquinazoline F, and fiscalin B promoted by microwave irradiation. *J Organ Chem.* 2005;70:6339–45.

<http://dx.doi.org/10.1016/j.pbj.2017.07.114>

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