± 0.0187; p=10^-6). However, unlike lymphocytes, the cytotoxic effects of cladribine on monocytes were not sustained, and the cells repopulated at 2 months post-cladribine treatment. Extended analysis of monocyte subtypes showed a reduction in the 'non-classical' monocyte (CD14-CD16+) subset at 1-week post-cladribine treatment. However, this was not reflected in the 'classical' (CD14+CD16-) and 'intermediate' (CD14+CD16+) monocyte populations.

Conclusion This study demonstrates a novel mechanism of action for Cladribine, highlighting that it exerts its effects acutely on peripheral monocytes. The laboratory data will be linked to clinical data to decipher what innate immune parameters translate to better patient outcome.

2305 GLIOBLASTOMA – INHIBITION OF P2X7R AS A POTENTIAL THERAPEUTIC TARGET FOR TREATMENT OF THIS AGGRESSIVE CANCER

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Introduction The most common and most lethal form of primary brain cancer is glioblastoma. With current treatments, prognosis of patients with glioblastoma remains poor: average survival of 10–18 months. P2X7R is a purinergic receptor and has roles in cell trophism and innate immunity, and has been implicated in glioblastoma.

Objectives To investigate P2X7R expression, function and its antagonism in human glioblastoma.

Methods The U251 glioblastoma cell line, patient-derived primary glioblastoma cultures, and glioblastoma stem cells were utilized. P2X7R expression was assessed using immunohistochemistry and qPCR. P2X7R function was assessed using confocal microscopy, Fluo4 AM calcium imaging, and YOPRO1 and ethidium bromide nuclear uptake experiments. Cell proliferation and cell death was quantified using DAPI stain cell counts, as well as annexin V (apoptosis) and LDH release (necrosis).

Results P2X7R is expressed in glioblastoma U251 cells, as well as human-derived glioblastoma tumour cells and microglia, and glioblastoma stem cells. The receptor is functional in each setting. Inhibition of the receptor with AZ10606120 decreases cell number in U251cells, in primary glioblastoma cultures and in glioblastoma stem cells. The anti-tumour effect of AZ10606120 was significantly higher than the conventional chemotherapy Temozolomide (p<0.001).

Conclusion This study has identified P2X7R antagonism as a potential therapeutic target in the treatment of human glioblastoma. The outcomes of this study are to be used in a future phase I clinical trial assessing a P2X7R blockade as much needed therapy for this aggressive cancer.

2306 SEIZURE RISK IN MULTIPLE SCLEROSIS PATIENTS ON DISEASE MODIFYING THERAPIES: A SYSTEMATIC REVIEW AND NETWORK META-ANALYSIS

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Objective There is a two to three-fold increased prevalence of seizures in multiple sclerosis (MS) patients compared to the general population. Conflicting reports exist of seizures occurring as an adverse event in disease modifying therapies (DMTs) such as interferon, glatiramer acetate, and fingolimod; however, DMTs have also been postulated to have anti-epileptogenic effects. We aimed to evaluate the risk of seizures in MS patients on DMTs compared to placebo.

Methods MEDLINE (OVID), EMBASE, CINAHL, and ClinicalTrials.gov were searched to 21st August 2021. Two reviewers independently screened and extracted data from full-text papers for placebo-controlled randomised trials of DMT (s) as monotherapy in patients ≥18 years and appraised the risk of bias. The primary outcome was seizure risk ratio (SRR) in dose-pooled DMT-treated patients compared to placebo. Meta-analyses and network meta-analyses (NMA) were performed using 'R'.

Results 331 of 1509 screened studies underwent full-text eligibility review. 56 studies were included, comprising 29,388 patients randomised to placebo (n=10,479) or DMT (n=18,909). 60 seizures were reported (DMT = 41, placebo = 19). Notably, 12 seizures occurred in one trial in patients treated with siponimod 2mg daily, corresponding to 1 seizure in 276.25 patient-exposed-years; no seizures were reported in other siponimod studies. Preliminarily, meta-analyses and NMA did not demonstrate a difference in SRR between DMT and placebo, nor increased SRR according to specific DMT.

Conclusion DMT use is not associated with increased seizure risk in MS patients, which can be incorporated in the counselling of patients commencing DMTs.

2307 LEGIONELLA PNEUMONIA AND POST-INFECTIOUS INFLAMMATORY POLYNEUROPATHY

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Neurological manifestations of Legionella infection were widely reported in the 1970s after the bacterium, Legionella pneumophilia, was first identified. Most frequent are headache and delirium with only a few case reports describing peripheral neuropathy. Supportive neurophysiological and histopathological data in the literature is scant. We present the case of a 67 year-old female with legionella pneumonia complicated by painful polyneuropathy, with confirmation of inflammatory neuritis on sural nerve biopsy. It emphasises a perhaps under reported sequala of Legionella infection and