



A Systematic Review of Targeted Therapy for Neurofibromatosis Type-2 Mutated Vestibular Schwannomas

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BACKGROUND

Neurofibromatosis type 2 (NF2) is an autosomal dominant tumour pre-disposing syndrome caused by mutations in the NF2 gene. One of its hallmarks is bilateral vestibular schwannomas (VS) causing hearing loss.

AIM

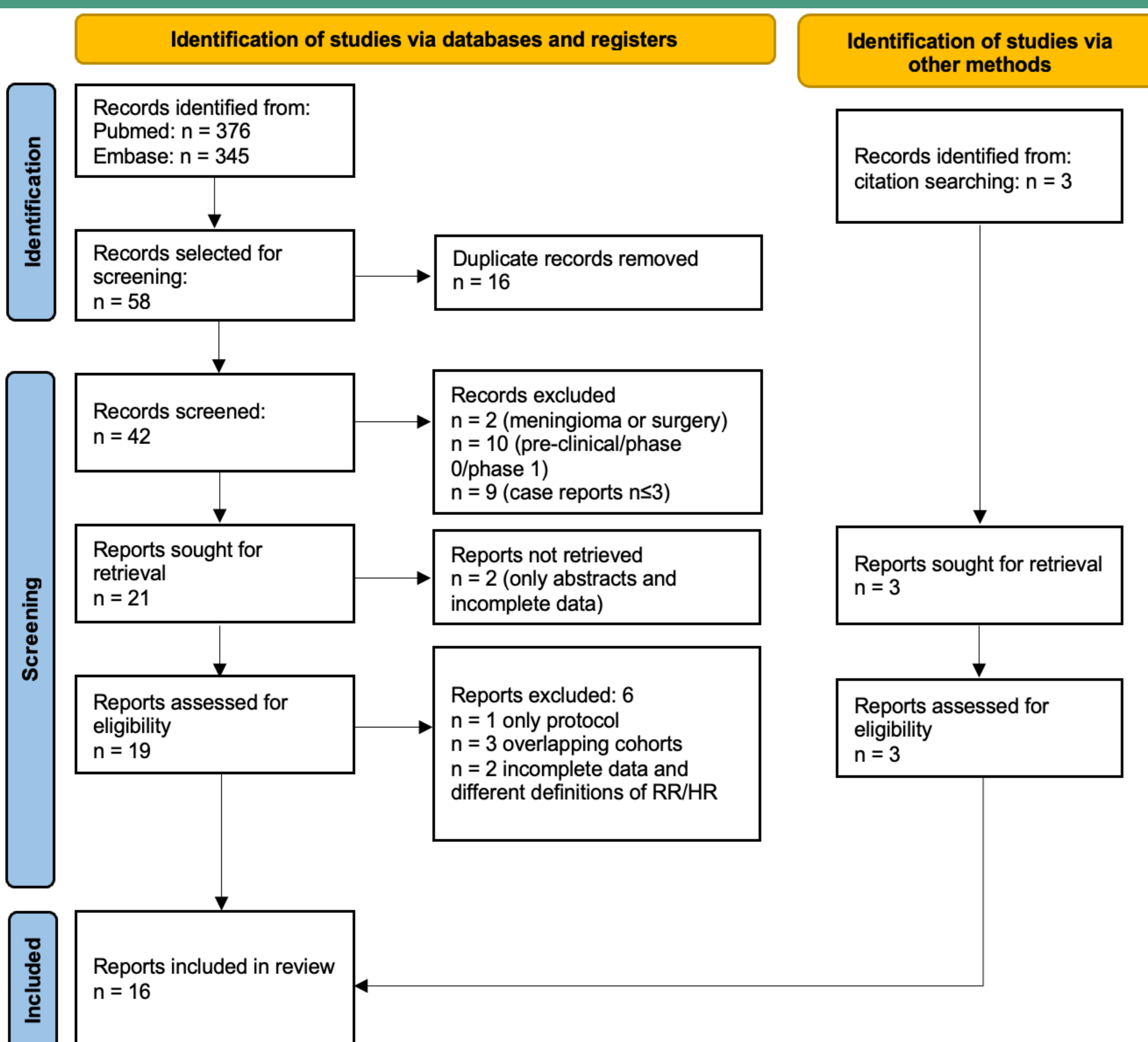
To summarize the clinical efficacy and safety of targeted agents when treating NF2 patients with VS.

METHODS

Primary outcome

- Radiographic response:** > 20% decrease in tumour volume,
- Hearing response:** Significant increase in word recognition scores

Figure 1: Selection process of the studies according to the PRISMA guidelines



RESULTS

Figure 2: Signalling pathways regulated by Merlin

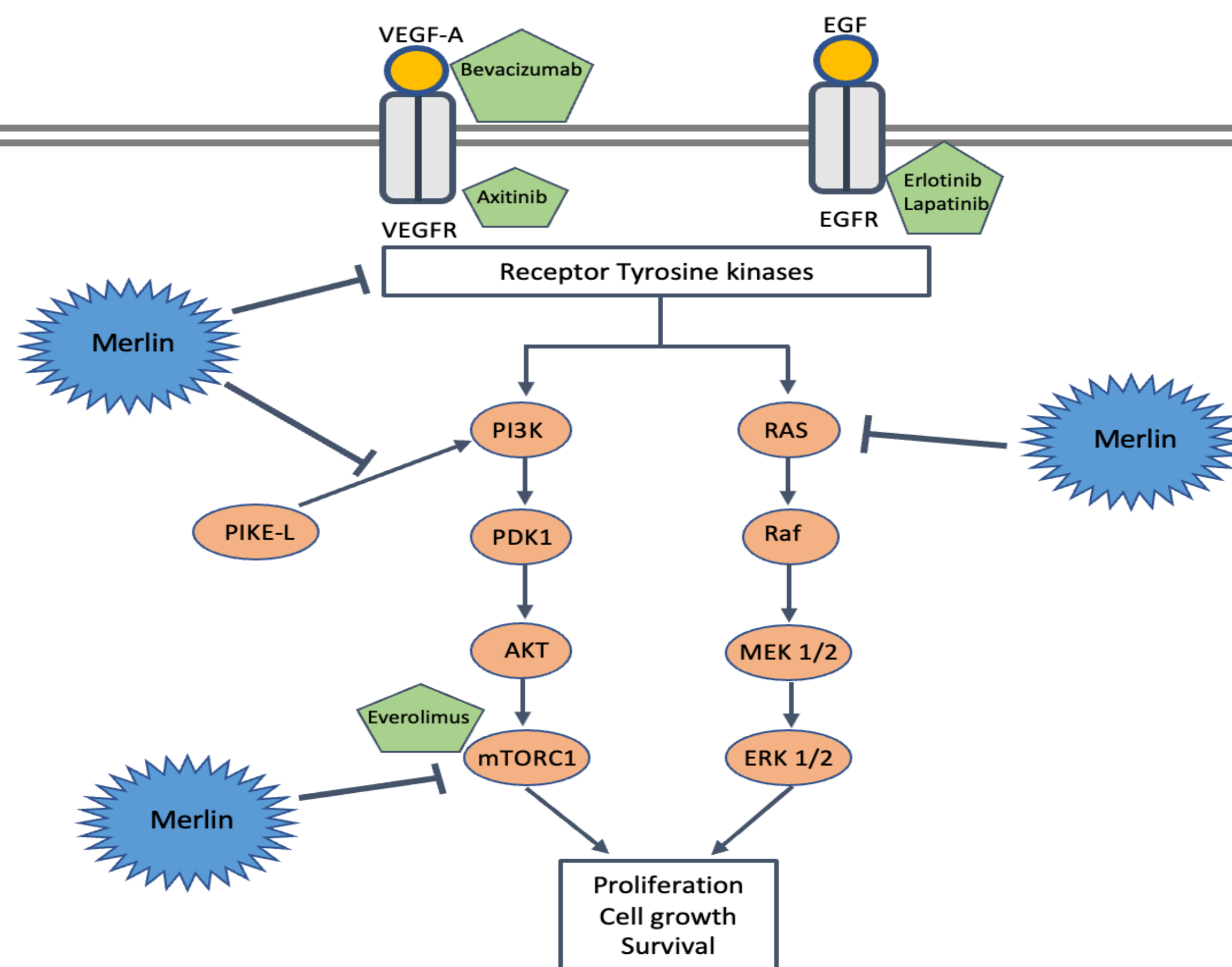


Table 1: Overview of studies investigating bevacizumab

Study	Cohort size	Dosage and scheduling	Radiographic response	Hearing response
Morris et al, 2016	61	5mg/kg/2 weeks	32%	45%
Blakeley et al, 2016	14	7.5 mg/kg/3 weeks	43%	36%
Plotkin et al, 2019	22	10 mg/kg/2 weeks	32%	41%
Alanin et al, 2014	12	10 mg/kg/2 weeks	50%	33%
Plotkin et al, 2012	31	5 mg/kg/2 weeks	55%	57%
Farschtschi et al, 2015	3	5 mg/kg/2-3 weeks	100%	0%
Goutagny et al, 2016	16	5 mg/kg/2 weeks	36%	NR
Hochart et al, 2014	7	5-10 mg/kg/2 weeks	14%	25%
Sverak et al, 2019	17	5-10 mg/kg every 2-6 weeks	47%	56%
Renzi et al, 2019	17	5-10 mg/kg/2-3 weeks	12%	62%
Pooled data (95% CI)	200*	5-10 mg/kg/2-3 weeks	38% (32 – 45)	45% (36 – 54)

Table 2: Overview of studies investigating other drugs

Study and drug	Cohort size	Radiographic response	Hearing response
Karajannis et al, 2013, Everolimus	10	0%	0%
Goutagny et al, 2014, Everolimus	10	0%	0%
Karajannis et al, 2012, Lapatinib	21	6%	31%
Plotkin et al, 2010, Erlotinib	11	0%	17%
Tamura et al, 2019, VEGFR vaccine	7	29%	40%
Phadnis et al, 2020, Axitinib	12	17%	25%

CONCLUSION

- Bevacizumab was the most effective targeted treatment
 - Hearing response rate of 45% (36 – 54)
 - Radiographic response rate of 38% (32 – 45)
 - The most common grade 3-4 toxicities were hypertension, proteinuria and menorrhagia
- A lower bevacizumab dosage (5mg/kg), compared to a higher dosage (10mg/kg) showed similar efficacy and was associated with lower toxicity
- Other targeted agents, like lapatinib and the VEGF receptor vaccine showed some activity