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# Benchmarking the Efficacy of Salvage Systemic Therapies for Recurrent Meningioma: A RANO Group Systematic Review and Meta-analysis to Guide Clinical Trial Design

Rupesh Kotecha<sup>1</sup>, Eyub Y Akdemir<sup>1 2</sup>, Tugce Kutuk<sup>1</sup>, Can Ilgin<sup>3</sup>, Manmeet S Ahluwalia<sup>4</sup>, Wenya L Bi<sup>5</sup>, Jaishri Blakeley<sup>6</sup>, Karan S Dixit<sup>7</sup>, Ian F Dunn<sup>8</sup>, Evanthia Galanis<sup>9</sup>, Norbert Galldiks<sup>10</sup>, Raymond Y Huang<sup>11</sup>, Derek R Johnson<sup>12</sup>, Thomas J Kaley<sup>13</sup>, David O Kamson<sup>14</sup>, Sylvia C Kurz<sup>15</sup>, Michael W McDermott<sup>16</sup>, Yazmin Odia<sup>17</sup>, Matthias Preusser<sup>18</sup>, Jeffrey Raizer<sup>7</sup>, David A Reardon<sup>19</sup>, C Leland Rogers<sup>20</sup>, Roberta Ruda<sup>21</sup>, David Schiff<sup>22</sup>, Michael A Vogelbaum<sup>23</sup>, Michael Weller<sup>24</sup>, Patrick Y Wen<sup>25</sup>, Minesh P Mehta<sup>1</sup>

Affiliations

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## Abstract

**Background:** Despite advances in our understanding of the molecular underpinnings of meningioma progression and innovations in systemic and local treatments, recurrent meningiomas remain a substantial therapeutic challenge. The objective of this systematic review and meta-analysis is to provide a historical baseline, contemporary analysis, and propose a "rate of probable interest" to inform future clinical trial design and development on behalf of the RANO meningioma group.

**Methods:** PubMed, ClinicalTrials.gov, and ASCOpubs databases were screened for clinical trials evaluating the activity of systemic therapies for adults with recurrent meningiomas. The pooled progression-free survival at 6-months and 1-year (PFS-6 and PFS-1 year) values were calculated using the random effects technique with I-squared indices.

**Results:** The pooled PFS-6 and PFS-1 year rates for recurrent WHO grade 1 meningiomas were 43.6% (95% CI: 22.7-67.0%, I<sup>2</sup>=80%) and 21.7% (95% CI: 6.2-53.9%, I<sup>2</sup>=76%), and for grade 2-3 meningiomas, the PFS-6 was 38.0% (95% CI: 28.3-48.8%, I<sup>2</sup>=68%). In targeted therapy group, PFS-6 and PFS-1 year rates stood at 62.0% (I<sup>2</sup>=58%) and 49.0% (I<sup>2</sup>=63%) for grade 1, while for grade 2-3 tumors, the PFS-6 rate with targeted therapy and immunotherapy was 42.1% (I<sup>2</sup>=60%) and 46.0% (I<sup>2</sup>=0%), respectively. The benchmarks were set at 67% and 54% for PFS-6 and PFS-1 year for grade 1 tumors, and PFS-6 of 49% for grade 2-3 tumors.

**Conclusions:** Several studies have reported outcomes in patients with recurrent meningiomas testing a variety of agents with modest, but variable and progressively increasing activity. In this context, we recommend new benchmarks for future trials to define efficacy of future investigational therapies.

**Keywords:** clinical trials; meningioma; recurrent; refractory; systemic therapy.

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