

CURRENT CLINICAL STUDIES THAT SHOW EFFICIENCY IN PRIMARY BRAIN TUMOURS: AN OVERVIEW

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Introduction & Aim

Brain cancer is one of the most difficult-to-treat cancers. In spite of the advances in anticancer drug development during the last decade, the treatment outcome of patients remains unchanged. Only a handful of current anticancer drugs are approved against any type of brain tumour. (Figure 1)

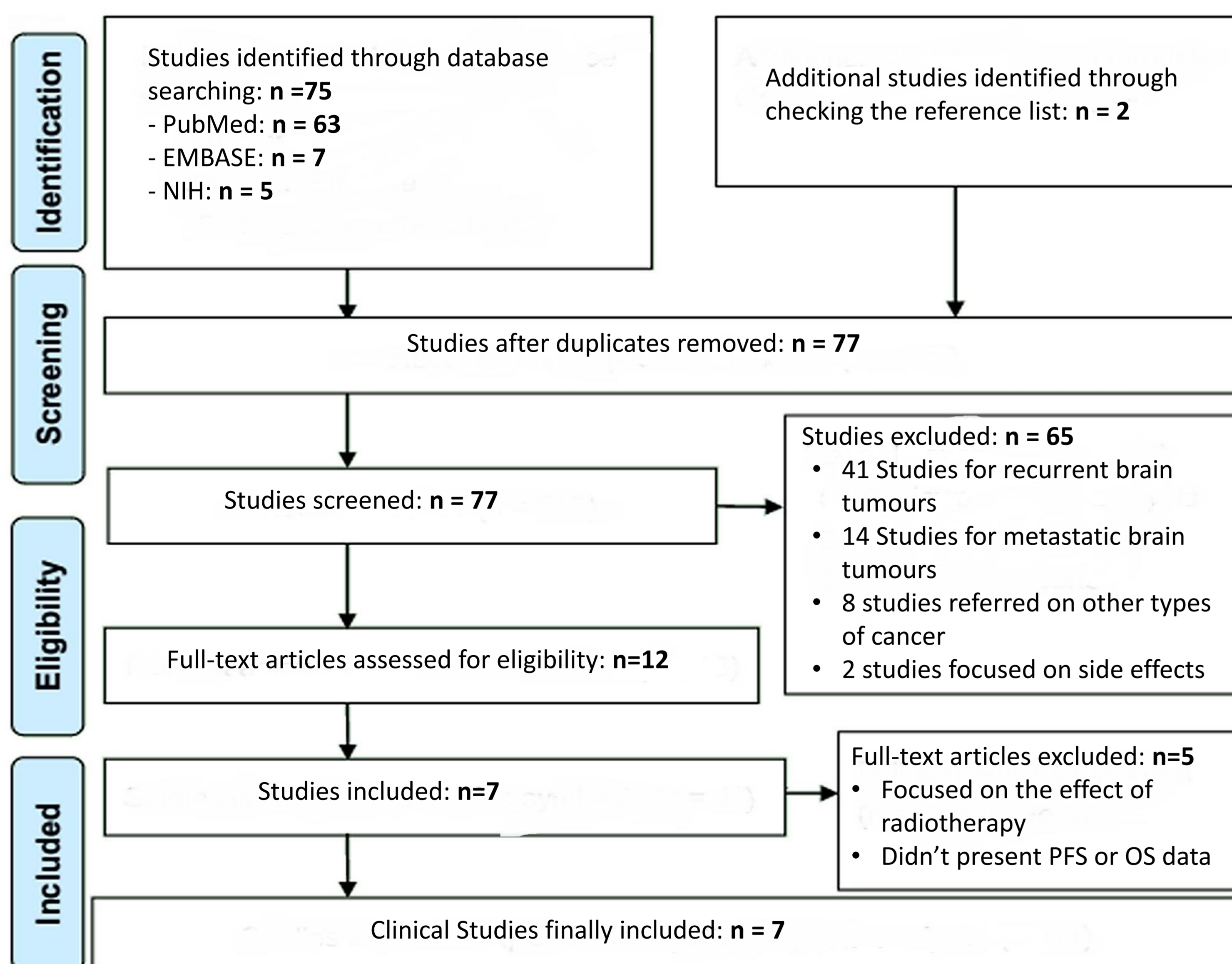
In this study, we aimed to survey and identify the chemotherapeutic drugs involved in clinical trials during the last decade in case of newly diagnosed primary brain tumours and describe the available evidence for the treatment.

Chemotherapeutic drugs that are approved form FDA for the treatment of primary brain tumours
1. Temozolomide
2. Bevacizumab
3. Everolimus
4. Carmustine
5. Lomustine
Combination of chemotherapeutic drugs that used for the treatment of primary brain tumours
PCV (Procarbazine + Lomustine + Vincristine)

Figure 1. Table listing the drugs used in the chemotherapy of brain tumors (reference: National Cancer Institute)

Methods

We applied a methodological advanced search of clinical trials in Phase II and III of the last decade that involve chemotherapy, using various electronic databases of clinical studies that are linked to the FDA, for all types and subtypes of brain tumours. We focus only on newly diagnosed primary brain tumours. Thus, we excluded clinical trials that were referred on recurrent or metastatic brain tumours. Median progression-free survival (PFS) period and median overall survival (OS) period were used as the primary common endpoints for comparing efficacy. Moreover, we excluded studies that were terminated before integration.



Main Results

Main drugs used in clinical trials for newly diagnosed primary brain tumours with positive data, without possessing an indication for this type of cancers
1. Irinotecan
2. Erlotinib
3. Gefitinib

Figure 2. This table presents drugs that do not hold approval for use in the treatment of primary brain tumours but they are indicated against other types of malignancies. These drugs have been used in a number of Phase II or III clinical trials during the last ten years in combination with other chemotherapeutic drugs or radiotherapy for the treatment of newly diagnosed primary brain tumours.

Clinical trials for newly diagnosed primary brain tumours (2007 – 2017)						
Type of Primary Brain Tumour	Clinical trial phase	Drugs or drug combination used	Evidence		Clinical Study ID	Reference
			PFS period	OS period		
Anaplastic oligodendroglioma	III	PCV + RT	-	14.7 Years	NCT00002569	Cairncross, 2013
	III	Bevacizumab + Temozolomide + RT	12 months	24 months	NCT00943826	Chinot, 2011
Glioblastoma (GBM)	II	Bevacizumab + Irinotecan + Temozolomide	-	12 months	NCT00979017	Peters, 2015
	II	Carmustine + Temozolomide + RT	-	20.2 months	NCT00919737	Tomokazu, 2014
	II	Erlotinib + Temozolomide + RT	-	19.3 months	PMC2645859	Prados, 2009
	II	Bevacizumab + Erlotinib + Temozolomide + RT	13.5 months	19.8 months	PMC4057142	Clarke, 2014
	II	Gefitinib + RT	4.9 months	11.5 months	PMC4199329	Chakravarti, 2013

Figure 3. Collective data regarding current clinical studies that use new combinations of drugs as part of the designed pharmacotherapy that aim to improve the therapeutic result in patients with non-recurrent primary brain tumours. We include studies that their efficacy was reported based on median progression free survival (PFS) period or on median overall survival (OS) period. One of the most promising combination for the treatment of newly diagnosed glioblastoma (according to the published data from the above clinical trials) is Bevacizumab + Temozolomide + Radiotherapy (RT), which PFS period reported at 12 months and the OS period reported in 24 months.

Main Conclusions

There is a small number of approved drugs that currently have an indication for brain cancer. It is therefore very important that newer drugs or drug combinations are tested for increased efficacy through clinical trials for primary brain tumours. A number of possible drug combinations with existing chemotherapeutic drugs currently used against other type of tumours have shown increased efficacy in the treatment of several primary brain tumours, compared to standard therapy. Furthermore, there is a small number of clinical trials focus on newly diagnosed primary tumours in comparison with clinical trials studied recurrent brain tumours.

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