

Table II. Comparison of the results of standard therapy with antineoplastic agents A10 and AS2-1 in all patients with primary brain tumours

Study	Drugs	No. of evaluable cases	Histopathology of the tumours (%)					Response (%)				MTP (mo)	MST (mo)
			GBM	AG	LG	OT	CR	PR	SD	PD			
Sandberg-Wollheim et al. ^[23]	PCV + RA	68	4	96								6.7	14.2
Jeremic et al. ^[24]	CBDCA + etoposide (VP-16)	38	79	21			21	32	47			3.2	9.9
Hildebrand et al. ^[25]	Dibromodulcitol, carmustine (BCNU) + RA	127	73	14	14 ^a							8.0	12.9
Couldwell et al. ^[26]	Tamoxifen	32	62.5	37.5		3.1	21.9	18.8	56.2				10.1
Yung et al. ^[26]	13-cis-retinoic acid	43	35	49	16		7	46.5	46.5			3.7	11.9
Burzynski et al. (CAN-1 study)	Antineoplastic agents A10 and AS2-1	36	39	36	14	11 ^b	25	19.5	33.3	22.2		15.8	27.1

a Anaplastic ependymoma, oligodendroglioma, oligoastrocytoma and gliosarcoma.

b Primitive neuroectodermal tumour, malignant meningioma.

AG = anaplastic glioma; astrocytoma, oligodendroglioma, mixed glioma; CBDCA = 1-cyclobutane-dicarboxylatoplatinum II; CR = complete response; GBM = glioblastoma multiforme; LG = low grade astrocytoma, oligodendroglioma, mixed glioma; MST = median time of survival from first day of treatment; MTP = median time to progression from first day of treatment; OT = other tumours; PCV = procarbazine, CCNU (lomustine), vincristine; PR = progressive disease; PD = partial response; RA = radiation therapy; SD = stable disease.

inhibition of farnesylation of the p21^{ras} protein and causes downregulation of Bcl-2.^[18,19]

PN also increases the expression of the p53 tumour suppressor gene. Activation of the p53 system involves increasing both the expression of the WAF1 gene and formation of the p21^{WAF1} protein, which demethylate promoter sequences of tumour suppressor genes.^[20-21]

In vitro studies also have shown that PG and isoPG have antineoplastic activity and that their mechanisms appear to differ from that of PN. The neoplastic process results from over-expression of oncogenes and decreased expression of tumour suppressor genes. Regulation of the expression of these genes by PN and related compounds may create a new approach to gene therapy.

The results of this study indicate that of 16 patients classified as complete and partial responders, 11 are alive today. In addition, another four patients classified as having stable disease are still alive today. Most of the surviving patients have now been alive for over 3½ years from the beginning of antineoplastic therapy. One patient with astrocytoma has been alive for over 11 years since starting antineoplastic therapy, despite a life expectancy of less than 6 months upon admission.

The largest group of 14 patients involved in the CAN-1 study was diagnosed with GBM. Of these patients, two were classified as complete responders and three as partial responders, four obtained stabilisation, and five developed disease progression. Of these 14 patients, two are alive today; one has been tumour-free for over 6 years.

In the next largest group of 13 patients with anaplastic glioma, there were four complete and two partial responses, five cases of stable disease, and two cases of progressive disease. Six patients are alive today.

A small group of five patients were diagnosed with low grade astrocytoma, oligodendroglioma, or mixed glioma. One obtained complete response, two partial response, and two stable disease. All five patients are alive today, with one having disease progression.