Supplementary Online Content

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This supplementary material has been provided by the authors to give readers additional information about their work.

eTable 1. Included Study Characteristics

eTable 1. Inc	Level of	Years	N each	Extent of	Median	Adjuvant
year	evidence	of	group	resection	follow	therapies
<i>y</i>		patient	8 F	determination	up	F
		accrual				
Ahmadloo	IV	1990-	GTR:	MRI/CT GTR	11 mos	RT, PCV, T
2013		2008	15	>98%		, ,
			STR:	resection		
			150			
			Bx: 58			
Albert 1994	IV	1989-	GTR:	CT/MRI EOR	15 mos	RT
		1994	72	ND		
			STR:			
			31			
Ammirati	IV	NS	GTR:	MRI	NS	RT, Ch
1987			19	GTR= no		
			STR:	residual		
			12	enhancement		
Butowski	III	1975-	GTR:	MRI	NS	Ch, Br
2007		2003	153	GTR> 90%		
			STR:	resection of		
			740	enhancing		
				tissue		
Chaichana	III	1997-	STR:	Defined by	NS	RT, T
2011		2007	40	procedure		
			Bx: 40			
Chaichana	III	2007-	STR:	Defined by	NS	RT, T
2014		2012	29	procedure		
			Bx: 19			
Dea 2012	IV	2004-	GTR:	MRI.	NS	RT, T, Ch
		2008	27	GTR>90%		
			STR:95	reduction		
Devaux	IV	1984-	STR:	Defined by	NS	RT
1993		1988	63	procedure		
			Bx: 86			
Ewelt 2011	IV	2002-	GTR:	MRI	NS	RT, Ch, T
		2007	23	GTR = no		
			STR:	residual		
			37	enhancement		
			Bx: 43			
Hrabalek	II	2007-	GTR: 3	MRI	NS	RT + T
2015		2009	STR:	GTR >99%		
			19	resection of		
			Bx: 16	enhancing		
				tissue		

Jeremic	III	1988-	GTR or	Defined by	NS	RT +
1994		1991	STR:	procedure. No		PCV/BCNU+H
			61	definition for		
			Bx: 25	GTR		
Kalita 2014	IV	2006-	GTR or	Defined by	NS	RT, T
		2012	STR:	procedure		
			63	Surgery >		
			Bx: 68	70% resection		
Keles 1999	III	1980-	GTR:	MRI	NS	RT, Ch
		1991	20	GTR = no		
			STR:	residual		
			54	enhancement		
Kelly 1994	III	1984-	STR:	Defined by	NS	RT
		1992	40	procedure		
			Bx: 88			
Kiwit 1996	IV	1986-	GTR:	Surgeon's	NS	RT
		1990	26	opinion. CT		
			STR:	and MRI		
			28			
			Bx: 36			
Kreth 1993	III	1986-	STR:	Defined by	35.6 w	RT
		1991	57	procedure		
77 1 1000		1001	Bx: 58	- a 11		200
Kreth 1999	II	1991-	STR:	Defined by	Until	RT
		1994	126	procedure	death	
			Bx: 99		(all	
					died by	
Kreth 2013	III	2004-	GTR:	MRI	1999) NS	RT, At, T
Kieui 2013	111	2004-	125	GTR = no	110	K1, At, 1
		2009	STR:	residual		
			148	enhancement		
			Bx: 72	Cimanecinent		
Study and	Level of	Years	N each	Extent of	Median	Adjuvant
year	evidence	of	group	resection	follow	therapies
3		patient	8 F	determination	up	
		accrual				
Kuhnt 2011	IV	2002-	GTR:	MRI	NS	RT, Ch
		2008	79	GTR = no		
			STR:	residual		
			56	enhancement		
Li 2015	II	1993-	GTR:	MRI	NS	NS
		2012	876	GTR = no		
			STR:	residual		
			353	enhancement		
Martinez	IV	1999-	GTR:	MRI	NS	NS

2007		2004	64 STR: 38	GTR = no residual enhancement		
McGirt	III	1996-	BX: 25 GTR:	MRI	18 mos	RT, G, T
2009		2006	330 STR: 619	GTR = no residual enhancement		
Nitta 1995	IV	1988- 1994	GTR: 14 STR: 54	CT GTR = no residual enhancement	NS	NS
Noorbakhsh 2014	III	1998- 2009	GTR: 6018 STR: 5609 Bx: 3982	Surgical code according to SEER handbook	NS	RT, Ch, T
Oszvald 2012	III	2000- 2006	GTR: 60 STR: 174 Bx: 127	MRI GTR = no residual enhancement		RT, Ch, T, ACNU
Pichlmeier 2008	II	1999- 2004	GTR: 122 STR: 121	MRI GTR = no residual enhancement	35.4 mos	RT
Pirotte 2009	IV	1997- 2004	GTR: 10 STR: 21	MRI/PET GTR = no residual enhancement	Until death	NS
Salvati 2012	IV	2002- 2007	GTR: 45 STR: 34 Bx: 25	MRI GTR = no residual enhancement	NS	RT, Ch, T
Senft 2010	IV	2004- 2005	GTR: 29 STR: 12	MRI GTR = no residual enhancement	82 wks	RT, Ch, T
Shinoda 2001	III	1989- 1998	GTR: 36 STR: 36	MRI GTR = no residual enhancement	Until death	RT, ACNU, IFNB, Cis
Simpson 1993	III	1974- 1987	GTR: 105	Surgeon impression	NS	RT, BCNU, MeCCNU

		I			I	T
			STR:			
			413			
			Bx: 107			
Stark 2005	IV	1990-	GTR:	CT	NS	RT, Ch, T, Cis,
		2001	167	GTR = no		ACNU
			STR:	residual		
			199	enhancement		
Stummer	IV	1995-	GTR:	MRI	NS	RT, Ch, Br
2000		1998	33	GTR = no		, - ,
			STR:	residual		
			19	enhancement		
Uzuka 2012	III	2000-	STR:	CT or MRI	12 mos	ACNU,
02aka 2012		2010	73	GTR = >90%	12 11105	MeCCNU, T
		2010	Bx: 34	reduction of		Meceric, 1
			DA. 31	enhancing		
				tissue		
Vuorinen	III	1992-	STR:	Defined by	Until	RT
2003	111	2006	14	procedure	death	KI
2003		2000	Bx: 16	procedure	ueam	
Study and	Level of	Years	N each	Extent of	Median	Adjuvant
Study and	evidence	of		resection	follow	•
year	evidence	_	group	determination		therapies
		patient		determination	up	
37 1 '	13.7	accrual	CTD	MDI	21	A CINITI C. T
Yamaguchi	IV	2000-	GTR:	MRI	21 mos	ACNU, Cis, T
2012		2011	60	GTR = no		
			STR:	residual		
			69	enhancement		
			Bx: 31			
Zinn 2013	IV	1973-	GTR:	Surgical code	NS	RT, Ch
		2007	4981	according to		
			STR:	SEER		
			8753	handbook		
			Bx:			
			3197			

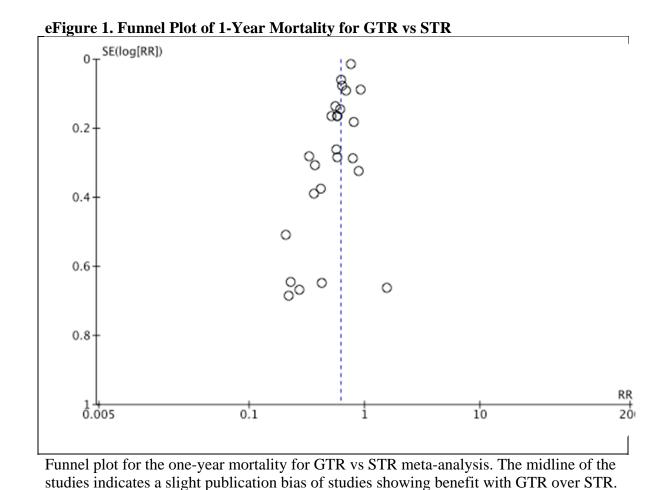
eTable 1. Demographic characteristics of all studies that were included in at least one comparison. Key: GTR, Gross total resection as defined in the individual studies STR, subtotal resection Bx, biopsy, NS, Not stated ND, Not Defined RT, Radiation therapy PCV, procarbazine, cisplatin, vincristine, T, temozolomide, Ch, chemotherapy not otherwise specified, Br, brachytherapy, BCNU, carmustine, H, hydroxyurea, At, Alkylating therapy, not otherwise stated, G, gliadel wafer, ACNU, nimustine, IFNB, interferon-beta, Cis, cisplatin MeCCNU, semustine

eTable 2. Subgroup Meta-analysis Results

Comparison	RR	RR	RR	RR only	RR only	RR only
	overall	without	without	Class II	studies	studies
		SEER	SEER	studies	since	since
			and		2005	2000
			RTOG			
1 yr RR	0.62	0.60	0.59	0.62	NA	0.53
mortality	[0.56-	[0.53-	[0.53-	[0.55-		[0.43-
GTR vs STR	0.69]	0.67]	0.65]	0.69]		0.67]
	p<0.001	p<0.001	p<0.001	p<0.001*		p<0.001
2 yr RR	0.84	0.83	0.82	0.72	NA	0.84
mortality	[0.79-	[0.77-	[0.76-	[0.49-		[0.79-
GTR vs STR	0.89]	0.89]	0.89]	1.07]		0.91]
	p<0.001	p<0.001	p<0.001	p=0.11*		p<0.001
1 yr RR	0.85	0.85	0.86	0.89	0.85	0.84
mortality STR	[0.80-	[0.78-	[0.79-	[0.78-	[0.68-	[0.71-
vs Bx	0.91]	0.92]	0.93]	1.01]	1.07]	1.00]
	p<0.001	p<0.001	p<0.001	p=0.06**	p=0.17	p=0.05
2 yr RR	0.99	0.99	1.00	0.92	0.92	1.00
mortality STR	[0.97-	[0.96-	[0.98-	[0.65-	[0.73-	[0.96-
vs Bx	1.00]	1.01]	1.01]	1.30]	1.18]	1.03]
	p=0.07	p=0.2	p=0.72	p=0.63**	p=0.53	p=0.77
1 yr RR	0.77	0.76	0.76	0.89	0.91	0.69
mortality Any	[0.71-	[0.69-	[0.68-	[0.78-	[0.75-	[0.58-
vs Bx	0.84]	0.84]	0.85]	1.01]	1.10]	0.82]
	p<0.001	p<0.001	p<0.001	p=0.06**	p=0.32	p<0.001
2 yr RR	0.94	0.96	0.97	0.92	0.92	0.95
mortality Any	[0.89-	[0.92-	[0.93-	[0.65-	[0.73-	[0.89-
vs Bx	1.00]	0.99]	1.00]	1.30]	1.18]	1.01]
	p=0.04	p=0.02	p=0.05	p=0.63**	p=0.53	p=0.12

eTable 2. Results of meta-analysis when further analyzed. Studies since 2000 includes only studies which included patients after 2000. Studies since 2005 only includes studies that analyzed patients accrued after 2005. The SEER studies included Zinn 2013 and Noorbakhsh 2014. RTOG data was published in Simpson 1993

^{*}Only two class II studies were included in this analysis, Li 2015 and Pichlmeier 2008. **Only two class II studies were included in this analysis, Kreth 1999 and Hrabalek 2015. The same data were used in both comparisons at the respective timepoints.

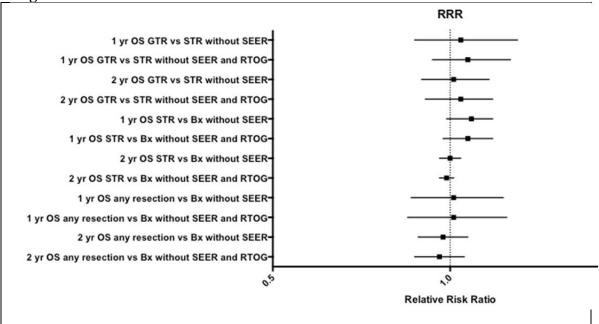


eFigure 2. RR of Mortality at 1 and 2 Years for Any Resection vs Biopsy

Study or Subgroup	Resec	tion	Biop	sv		Risk Ratio		Risk Ratio
study or subgroup	Events				Weight	M-H, Random, 95% CI	Year	M-H, Random, 95% CI
Kreth 1993	41	57	47	58	5.5%	0.89 [0.72, 1.09]	1993	-
Devaux 1993	39	63	69	86	5.2%	0.77 [0.62, 0.96]	1993	
Simpson 1993	313	538	82	107	6.9%	0.76 [0.67, 0.86]	1993	-
eremic 1994	23	61	21	25	3.2%	0.45 [0.31, 0.65]		
Kelly 1994	31	40	78	88	5.8%	0.87 [0.73, 1.05]		-
Kiwit 1996	26	54	29	36	3.7%	0.60 [0.43, 0.82]		
Kreth 1999	99	126	85	99	7.0%	0.92 [0.81, 1.03]		
Vuorinen 2003	8 63	10 102	13 17	13	3.5% 2.9%	0.80 [0.57, 1.12]		
Martinez 2007 Ewelt 2011	34	60	42	39 43	5.1%	1.42 [0.96, 2.09] 0.58 [0.46, 0.73]		
Chaichana 2011	34	40	35	40	6.0%	0.97 [0.82, 1.16]		
Uzuka 2012	27	73	17	34	2.4%	0.74 [0.47, 1.16]		
Salvati 2012	36	79	25	25	4.8%	0.47 [0.36, 0.59]		
Oszvald 2012	106	234	83	127	5.7%	0.69 [0.57, 0.84]		
Yamaguchi 2012	16	129	9	30	1.2%	0.41 [0.20, 0.84]		
Zinn 2013	8787	13734	1992	2667	8.1%	0.86 [0.84, 0.88]		•
Creth 2013	106	273	44	72	4.9%	0.64 [0.50, 0.81]		
Ahmadloo 2013	121	223	40	58	5.4%	0.79 [0.64, 0.97]	2013	
Chaichana 2014	24	29	14	19	3.7%	1.12 [0.82, 1.54]		+-
Kalita 2014	58	89	31	42	4.9%	0.88 [0.70, 1.12]		-+
drabalek 2015	16	22	15	16	4.2%	0.78 [0.58, 1.03]	2015	-
Total (95% CI)		16036		3724	100.0%	0.77 [0.71, 0.84]		•
Total (95% CI) Total events	10008		2788					•
Total (95% CI) Total events Heterogeneity: Tau ² =	0.02; Ch	ni² = 83.	30, df =					0.2 0.5 1 2 Favours Resection Favours Biog
	0.02; Ch	ni² = 83.	30, df =					0.2 0.5 1 2 Favours Resection Favours Biop
Total (95% CI) Total events Heterogeneity: Tau ² =	0.02; Ch	$ni^2 = 83.$ $I(P < 0.0)$	30, df =	20 (P <				
Total (95% CI) Total events Heterogeneity: Tau ² = Test for overall effect: Study or Subgroup	Resect Events	ni ² = 83. l (P < 0.0	30, df = 00001) Biops Events	20 (P <	0.00001 Weight); t ² = 76%	Year	Favours Resection Favours Biop
Total (95% CI) Fotal events Heterogeneity: Tau ² = Fest for overall effect: Study or Subgroup Simpson 1993	Resect Events 469	ni ² = 83. L (P < 0.0	8iops Events	20 (P <	Weight 1	Risk Ratio M-H, Random, 95% CI 0.91 [0.86, 0.95]	1993	Favours Resection Favours Biop
Total (95% CI) fotal events Heterogeneity: Tau ² = Fest for overall effect: Study or Subgroup Simpson 1993 Greth 1993	Resect Events 469 57	tion Total	8iops Events 103 58	20 (P <	Weight 17.2% 7.4%	Risk Ratio M-H, Random, 95% CI 0.91 [0.86, 0.95] 1.00 [0.97, 1.03]	1993 1993	Favours Resection Favours Biop
Fotal (95% CI) Fotal events Heterogeneity: Tau ² = Fest for overall effect: Study or Subgroup Simpson 1993 Freth 1993 Devaux 1993	Resect Events 469 57 59	tion Total 538 57	8iops Events 103 58 78	20 (P < Total 107 58 86	Weight 7.2% 7.4% 6.4%	Risk Ratio M-H, Random, 95% CI 0.91 [0.86, 0.95] 1.00 [0.97, 1.03] 1.03 [0.94, 1.13]	1993 1993 1993	Favours Resection Favours Biop
Fotal (95% CI) Fotal events Heterogeneity: Tau ² = Fest for overall effect: Study or Subgroup Simpson 1993 (reth 1993 Devaux 1993 Gelly 1994	Resect Events 469 57 59 37	tion Total 538 57 63 40	8iops Events 103 58 78 86	20 (P <	Weight 7.2% 7.4% 6.4% 6.3%	Risk Ratio M-H, Random, 95% CI 0.91 [0.86, 0.95] 1.00 [0.97, 1.03] 1.03 [0.94, 1.13] 0.95 [0.86, 1.04]	1993 1993 1993 1994	Favours Resection Favours Biop
Fotal (95% CI) Fotal events Heterogeneity: Tau ² = Fest for overall effect: Study or Subgroup Firmpson 1993 Great 1993 Gevaux 1993 Celly 1994 eremic 1994	Resect Events 469 57 59 37 47	tion Total 538 57 63 40 61	8iops Events 103 58 78 86 25	20 (P < Total 107 58 86 88 25	Weight 7.2% 7.4% 6.3% 5.1%	Risk Ratio M-H, Random, 95% CI 0.91 [0.86, 0.95] 1.00 [0.97, 1.03] 1.03 [0.94, 1.13] 0.95 [0.86, 1.04] 0.78 [0.67, 0.91]	1993 1993 1993 1994 1994	Favours Resection Favours Biop
Fotal (95% CI) fotal events Heterogeneity: Tau ² = Fest for overall effect: Study or Subgroup Simpson 1993 Greth 1993 Devaux 1993 Kelly 1994 Greremic 1994 Greth 1999	Resect Events 469 57 59 37 47 126	tion Total 538 57 63 40 61 126	8iops Events 103 58 86 25 99	20 (P < Total 107 58 86 88 25 99	Weight 7.2% 7.4% 6.4% 6.3% 7.6%	Risk Ratio M-H, Random, 95% CI 0.91 [0.86, 0.95] 1.00 [0.97, 1.03] 1.03 [0.94, 1.13] 0.95 [0.86, 1.04] 0.78 [0.67, 0.91] 1.00 [0.98, 1.02]	1993 1993 1993 1994 1994 1999	Favours Resection Favours Biop
Fotal (95% CI) Fotal events Heterogeneity: Tau ² = Fest for overall effect: Study or Subgroup Simpson 1993 Greth 1993 Devaux 1993 Celly 1994 eremic 1994 Kreth 1999 Martinez 2007	Resect Events 469 57 59 37 47 126 17	tion Total 538 57 63 40 61 126 102	Biops Events 103 58 78 86 25 99	20 (P < Total 107 58 86 88 25 99 25	Weight 17.2% 7.4% 6.4% 6.3% 5.1% 7.6% 0.2%	Risk Ratio M-H, Random, 95% CI 0.91 [0.86, 0.95] 1.00 [0.97, 1.03] 1.03 [0.94, 1.13] 0.95 [0.86, 1.04] 0.78 [0.67, 0.91] 1.00 [0.98, 1.02] 2.08 [0.51, 8.43]	1993 1993 1993 1994 1994 1999 2007	Favours Resection Favours Biop
Fotal (95% CI) Fotal events Heterogeneity: Tau ² = Fest for overall effect: Study or Subgroup Simpson 1993 Kreth 1993 Devaux 1993 Kelly 1994 Greth 1999 Martinez 2007 Ewelt 2011	Resect Events 469 57 59 37 47 126 17 60	tion Total 538 57 63 40 61 126 102 60	Biops Events 103 58 78 86 25 99 2	20 (P < Total 107 58 86 88 25 99 25 43	Weight 1 7.2% 7.4% 6.4% 6.3% 5.1% 7.6% 7.4%	Risk Ratio M-H, Random, 95% CI 0.91 [0.86, 0.95] 1.00 [0.97, 1.03] 1.03 [0.94, 1.13] 0.95 [0.86, 1.04] 0.78 [0.67, 0.91] 1.00 [0.98, 1.02] 2.08 [0.51, 8.43] 1.00 [0.96, 1.04]	1993 1993 1993 1994 1994 1999 2007 2011	Favours Resection Favours Biop
Fotal (95% CI) Fotal events Heterogeneity: Tau ² = Fest for overall effect: Study or Subgroup Simpson 1993 (reth 1993 Oevaux 1993 (elly 1994 eremic 1994 (reth 1999 Martinez 2007 Evelt 2011 Chaichana 2011	Resect Events 469 57 59 37 47 126 17 60 37	tion Total 538 57 63 40 61 126 102	Biops Events 103 58 78 86 25 99 2 43 40	20 (P < Total 107 58 86 88 25 99 25 43 40	Weight 7.2% 7.4% 6.3% 5.1% 7.6% 0.2% 6.2%	Risk Ratio M-H, Random, 95% CI 0.91 [0.86, 0.95] 1.00 [0.97, 1.03] 1.03 [0.94, 1.13] 0.95 [0.86, 1.04] 0.78 [0.67, 0.91] 1.00 [0.98, 1.02] 2.08 [0.51, 8.43] 1.00 [0.96, 1.04] 0.93 [0.84, 1.02]	1993 1993 1993 1994 1994 1999 2007 2011 2011	Favours Resection Favours Biop
Fotal (95% CI) Fotal events Heterogeneity: Tau ² = Fest for overall effect: Study or Subgroup Simpson 1993 (reth 1993 Devaux 1993 Gelly 1994 eremic 1994 (reth 1999 Martinez 2007 Ewelt 2011 Chalchana 2011 Salvati 2012	Resect Events 469 57 59 37 47 126 17 60	tion Total 538 57 63 40 61 126 102 60 40 79	Biops Events 103 58 86 25 99 2 43 40 25	20 (P < Total 107 58 86 88 25 99 25 43	Weight 1 7.2% 7.4% 6.4% 6.3% 5.1% 7.6% 0.2% 7.4% 6.2% 6.6%	Risk Ratio M-H, Random, 95% CI 0.91 [0.86, 0.95] 1.00 [0.97, 1.03] 1.03 [0.94, 1.13] 0.95 [0.86, 1.04] 0.78 [0.67, 0.91] 1.00 [0.98, 1.02] 2.08 [0.51, 8.43] 1.00 [0.96, 1.04] 0.93 [0.84, 1.02] 0.94 [0.86, 1.02]	1993 1993 1993 1994 1994 1999 2007 2011 2011	Favours Resection Favours Biop
Fotal (95% CI) fotal events Heterogeneity: Tau ² = Fest for overall effect: Study or Subgroup Simpson 1993 Greth 1993 Devaux 1993 Gelly 1994 Feremic 1994 Greth 1999 Martinez 2007 Evelt 2011 Chalchana 2011 Salvati 2012 Gamaguchi 2012	Resect Events 469 57 59 37 47 126 17 60 37 73	tion Total 538 57 63 40 61 126 102 60 40	Biops Events 103 58 78 86 25 99 2 43 40	20 (P < Total 107 58 86 88 25 99 25 43 40 25	Weight 7.2% 7.4% 6.3% 5.1% 7.6% 0.2% 6.2%	Risk Ratio M-H, Random, 95% CI 0.91 [0.86, 0.95] 1.00 [0.97, 1.03] 1.03 [0.94, 1.13] 0.95 [0.86, 1.04] 0.78 [0.67, 0.91] 1.00 [0.98, 1.02] 2.08 [0.51, 8.43] 1.00 [0.96, 1.04] 0.93 [0.84, 1.02] 0.94 [0.86, 1.02] 0.95 [0.75, 1.21]	1993 1993 1993 1994 1994 1999 2007 2011 2011 2012 2012	Favours Resection Favours Biop
Fotal (95% CI) fotal events feterogeneity: Tau ² = Fest for overall effect: Study or Subgroup Simpson 1993 Kreth 1993 Devaux 1993 Celly 1994 Ferentic 1994 Kreth 1999 Martinez 2007 Ewelt 2011 Chalchana 2011 Salvati 2012 Camaguchi 2012 Desvald 2012	Resect Events 469 57 59 37 47 126 17 60 37 73	tion Total 538 57 63 40 61 126 102 60 40 79 129	Biops Events 103 58 78 86 25 99 2 43 40 25 22	20 (P < Total 107 58 86 88 25 99 25 43 40 25 30	7.2% 7.4% 6.4% 6.3% 7.6% 0.2% 7.4% 6.3%	Risk Ratio M-H, Random, 95% CI 0.91 [0.86, 0.95] 1.00 [0.97, 1.03] 1.03 [0.94, 1.13] 0.95 [0.86, 1.04] 0.78 [0.67, 0.91] 1.00 [0.98, 1.02] 2.08 [0.51, 8.43] 1.00 [0.96, 1.04] 0.93 [0.84, 1.02] 0.94 [0.86, 1.02] 0.95 [0.75, 1.21] 0.98 [0.90, 1.06]	1993 1993 1993 1994 1994 1999 2007 2011 2011 2012 2012	Favours Resection Favours Biop
Fotal (95% CI) Fotal events Heterogeneity: Tau ² = Fest for overall effect: Study or Subgroup Simpson 1993 (reth 1993 Devaux 1993 Gelly 1994	Resect Events 469 57 59 37 47 126 17 60 37 73 90 200	tion Total 538 57 63 40 61 126 102 60 40 79 129 234	Biops Events 103 58 78 86 25 99 2 43 40 25 22 111	20 (P < Total 107 58 86 88 25 99 25 43 40 25 30 127	7.2% 7.4% 6.4% 6.3% 7.6% 0.2% 6.2% 6.3% 6.6%	Risk Ratio M-H, Random, 95% CI 0.91 [0.86, 0.95] 1.00 [0.97, 1.03] 1.03 [0.94, 1.13] 0.95 [0.86, 1.04] 0.78 [0.67, 0.91] 1.00 [0.98, 1.02] 2.08 [0.51, 8.43] 1.00 [0.96, 1.04] 0.93 [0.84, 1.02] 0.94 [0.86, 1.02] 0.95 [0.75, 1.21]	1993 1993 1993 1994 1994 1999 2007 2011 2011 2012 2012 2012 2013	Favours Resection Favours Biop
Fotal (95% CI) Fotal events Heterogeneity: Tau ² = Fest for overall effect: Study or Subgroup Simpson 1993 Greth 1993 Devaux 1993 Gelly 1994 Greth 1999 Martinez 2007 Ewelt 2011 Chaichana 2011 Salvati 2012 Oszvald 2012 Shmadloo 2013	Resect Events 469 57 57 47 126 17 60 37 73 90 200 208	tion Total 538 57 63 40 61 126 102 60 40 79 129 234 223	Biops Events 103 58 78 86 25 99 2 43 40 25 22 111 54	20 (P < Total 107 58 86 88 25 99 25 43 40 25 30 127 58	7.2% 7.4% 6.4% 6.3% 5.1% 7.6% 0.2% 6.6% 3.3% 6.6% 6.6%	Risk Ratio M-H, Random, 95% CI 0.91 [0.86, 0.95] 1.00 [0.97, 1.03] 1.03 [0.94, 1.13] 0.95 [0.86, 1.04] 0.78 [0.67, 0.91] 1.00 [0.98, 1.02] 2.08 [0.51, 8.43] 1.00 [0.96, 1.04] 0.93 [0.84, 1.02] 0.94 [0.86, 1.02] 0.95 [0.75, 1.21] 0.98 [0.90, 1.06] 1.00 [0.93, 1.08]	1993 1993 1993 1994 1994 1999 2007 2011 2011 2012 2012 2012 2013 2013	Favours Resection Favours Biop
Fotal (95% CI) Total events Jeterogeneity: Tau² = Jest for overall effect: Jeterogeneity: Tau² = Jest for overall effect: Jeterogeneity: Tau² = Jest for overall effect: Jeterogeneity: Jest for	Resect Events 469 57 59 37 47 126 17 60 37 73 90 208 208	tion Total 538 57 63 40 61 126 102 60 40 79 129 234 223 273	Biops Events 103 58 78 86 625 99 2 43 40 25 22 111 54 59	20 (P < Total 107 58 86 88 25 99 25 43 40 25 30 127 58 72	7.2% 7.4% 6.4% 5.1% 7.6% 0.2% 6.6% 3.3% 6.6% 3.3% 6.6% 5.4%	Risk Ratio M-H, Random, 95% CI 0.91 [0.86, 0.95] 1.00 [0.97, 1.03] 1.03 [0.94, 1.13] 0.95 [0.86, 1.04] 0.78 [0.67, 0.91] 1.00 [0.98, 1.02] 2.08 [0.51, 8.43] 1.00 [0.96, 1.04] 0.93 [0.84, 1.02] 0.94 [0.86, 1.02] 0.95 [0.75, 1.21] 0.98 [0.90, 1.06] 1.00 [0.93, 1.08] 0.84 [0.74, 0.97]	1993 1993 1994 1994 1999 2007 2011 2012 2012 2012 2013 2013 2013	Favours Resection Favours Biog
Fotal (95% CI) Fotal eyents feterogeneity: Tau² = Fest for overall effect: Fest for overall	Resect Events 469 57 59 37 47 126 17 60 37 73 90 200 208 189 10923	tion Total 538 57 63 40 61 126 102 60 40 79 129 234 223 273 13734	8iops Events 103 58 78 86 25 99 2 43 40 0 25 22 111 54 59 2472	20 (P < Total 107 58 86 88 25 99 25 43 40 25 30 127 58 72 2667	7.2% 7.4% 6.4% 6.3% 5.1% 7.6% 0.2% 7.4% 6.6% 3.3% 6.6% 6.7% 7.4%	Risk Ratio M-H, Random, 95% CI 0.91 [0.86, 0.95] 1.00 [0.97, 1.03] 1.03 [0.94, 1.13] 0.95 [0.86, 1.04] 0.78 [0.67, 0.91] 1.00 [0.98, 1.02] 2.08 [0.51, 8.43] 1.00 [0.96, 1.04] 0.93 [0.84, 1.02] 0.94 [0.86, 1.02] 0.95 [0.75, 1.21] 0.98 [0.90, 1.06] 1.00 [0.93, 1.08] 0.84 [0.74, 0.97] 0.86 [0.85, 0.87]	1993 1993 1994 1994 1999 2007 2011 2012 2012 2012 2013 2013 2013 2014	Favours Resection Favours Biog

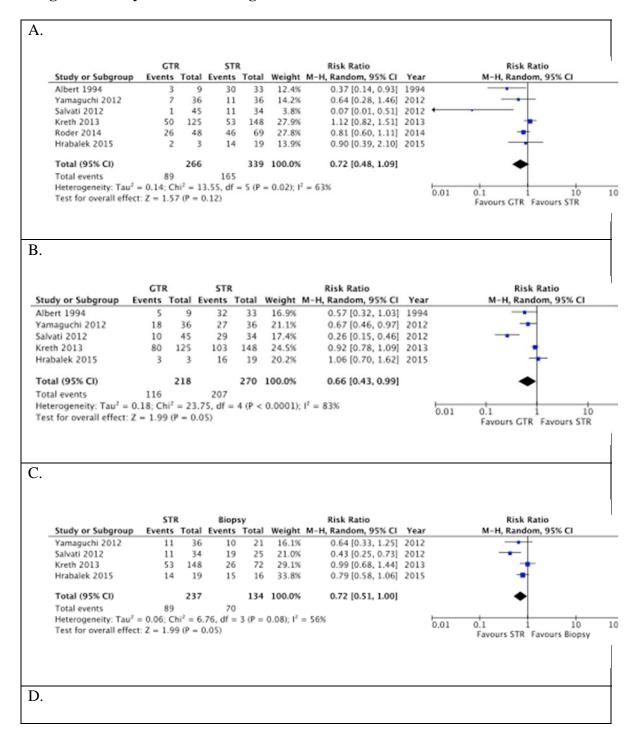
(A) One year RR mortality comparing any resection to biopsy. Twenty-one studies were included in this analysis of a total of 19 760 patients. The RR of mortality at one year is 0.77 (0.71-0.84), p<0.001 comparing any resection to biopsy. Removing SEER data, the RR of mortality at one year is 0.76 (0.69-0.84), p<0.001 with any resection compared to biopsy. (B) Two-year RR mortality comparing any resection to biopsy. This analysis of seventeen studies covers a total of 2994 patients. The RR of mortality at two years is 0.94 (0.89-1.00), p=0.04 comparing any resection to biopsy. Removing SEER data, the RR of mortality at two years is 0.96 (0.92-0.99), p=0.02 significantly favoring any resection over biopsy.

eFigure 3. Relative Risk Ratios



Relative risk ratios comparing relative risks of death at specific time points in the original meta-analysis and the repeated meta-analysis without SEER data (Zinn 2013, Noorbakhsh 2104) and without SEER and RTOG (Simpson 1993) data. This demonstrates inclusion of SEER and RTOG data insignificantly affects the overall meta-analysis and can be considered representative of the population and the body of literature.

eFigure 4. Analysis of RR of Progression-Free Survival



	Any Rese	ction	Biops	sy		Risk Ratio		Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	Year	M-H, Random, 95% CI
Jeremic 1994	13	61	16	25	12.0%	0.33 [0.19, 0.59]	1994	
Vuorinen 2003	8	10	13	13	15.5%	0.80 [0.57, 1.12]	2003	-
Yamaguchi 2012	18	72	10	21	11.4%	0.53 [0.29, 0.96]	2012	-
Oszvald 2012	117	234	78	127	17.5%	0.81 [0.67, 0.98]	2012	•
Salvati 2012	12	79	19	25	11.9%	0.20 [0.11, 0.35]	2012	
Kreth 2013	103	273	26	72	15.4%	1.04 [0.74, 1.47]	2013	+
Hrabalek 2015	16	22	15	16	16.3%	0.78 [0.58, 1.03]	2015	*
Total (95% CI)		751		299	100.0%	0.61 [0.44, 0.84]		•
Total events	287		177					2
Heterogeneity: Tau2 =	- 0.15; Chi	= 34.9	0, df = 6	(P < 0	.00001);	$I^2 = 83\%$		to 1
Test for overall effect	: Z = 3.01	P = 0.0	03)					0.01 0.1 1 10 Favours Any Resection Favours Biopsy
								ravours Any Resection Favours Biopsy

(A) RR of progression at six months, GTR vs. STR, not significantly favoring GTR. (B) RR of progression at one year, GTR vs STR. (C) RR of progression at six months, STR vs Bx. (D) RR of progression at 6 months for any resection vs Bx. All four of these analyses trended toward favoring more extensive resection, with all except the STR vs Bx comparison reaching significance. However, it is important to note that this topic is not as extensively studied as the relationship between overall survival and EOR. PFS was defined in the primary literature.