

HER2 positivity in histological subtypes of salivary gland carcinoma: A systematic review and meta-analysis

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Supplemental Data

S1: Overview of included studies and which data was included in meta-analysis

First Author	Year	Continent	Collection	HER2 Criteria	Probe IHC	ISH_type	Probe ISH	S D C	A D C	C EP	AD CC	A CC	Ba sal	Clea rC	E pi	Poo rly	Po ly	Muc oep	My oep	Onco cyt	Clea rC	SC C	Ly mfo	Intra duct	SDC IHC	SDC ISH
Khan	2001	America	Archival	IHC3	Novacastria	N/A	N/A	-	-	-	Yes	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Skálová	2001	Europe	Archival	IHC2 or IHC3	DAKO	N/A	N/A	Yes	Yes	Yes	Yes	Yes	Yes	-	-	Yes	-	Yes	Yes	-	-	-	-	-	-	-
Dori	2002	Asia	Archival	IHC3	DAKO	N/A	N/A	-	-	-	Yes	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Skalova	2003	Europe	Archival	IHC2 and ISH or IHC3	DAKO	FISH	Ventana	Yes	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	Yes	Yes
Glisson	2004	America	Archival	IHC2 or IHC3	DAKO	N/A	N/A	Yes	Yes	Yes	Yes	Yes	-	-	-	-	-	Yes	Yes	-	-	Yes	-	Yes	-	-
Weed	2004	America	Archival	IHC2 or IHC3	DAKO	N/A	N/A	-	-	-	-	-	-	-	-	-	-	Yes	-	-	-	-	-	-	-	-
Di Palma	2005	Europe	Archival	IHC3	Neomarkers	FISH	PathVysion	-	-	Yes	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Jaehne	2005	Europe	Archival	IHC3	DAKO	N/A	N/A	Yes	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	Yes	-
Cornolti	2007	Europe	Archival	IHC3 or ISH	DAKO	FISH	PathVysion	Yes	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	Yes	Yes
Nabili	2007	America	Archival	IHC3	DAKO	FISH	PathVysion	Yes	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	Yes
Tapia	2007	Europe	Na	IHC2 and ISH or IHC3	DAKO	FISH	PathVysion	-	Yes	-	-	Yes	-	-	-	-	-	Yes	-	-	-	Yes	-	-	-	-
Williams	2007	America	Archival	IHC3	Neomarkers	N/A	N/A	Yes	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	Yes	-
Ettl	2008	Europe	Archival	IHC2 or IHC3	DAKO	N/A	N/A	Yes	Yes	Yes	Yes	Yes	Yes	-	-	-	-	Yes	-	Yes	-	Yes	Yes	-	-	-
Shang	2008	Asia	Archival	IHC2 or IHC3	DAKO	N/A	N/A	-	-	-	-	-	-	-	-	-	-	Yes	-	-	-	-	-	-	-	-
Locati	2009	Europe	Archival	IHC2 and ISH or IHC3	DAKO	N/A	PathVysion	Yes	Yes	-	Yes	-	-	-	-	Yes	-	Yes	Yes	-	-	-	-	-	-	Yes
Luukka	2010	Finland and Canada	Archival	ISH	Ventana	SISH	Ventana	-	-	-	-	-	-	-	-	-	-	Yes	-	-	-	-	-	-	-	-
Williams	2010	America	Archival	IHC2 and ISH or IHC3	Labvision	FISH	PathVysion	Yes	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	Yes	Yes
Clauditz	2011	Europe	Archival	IHC3 or ISH	DAKO	FISH	PathVysion	Yes	Yes	-	Yes	Yes	Yes	-	Yes	-	Yes	Yes	Yes	Yes	-	-	-	-	Yes	Yes
Di Palma	2012	Europe	Archival	IHC2 and ISH or IHC3	DAKO	SISH	Ventana	Yes	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	Yes	Yes

S2: Search syntax

Searched up to 19th September 2020

PUBMED:

((salivary gland tumor[Title/Abstract] OR carcinoma of the salivary gland[Title/Abstract] OR salivary gland cancer[Title/Abstract])) AND (HER2 or c-ERB2)

Results: 37 hits

Web of science:

AB=(salivary gland tumor OR carcinoma of the salivary gland OR salivary gland cancer)

AND AB=(HER2 OR c-erbB2)

Results: 100 hits

EMBASE:

((salivary gland tumor or carcinoma of the salivary gland or salivary gland cancer).ab and HER2.af) or c-ERB2 af.

Results: 95 hits

S3: Full list of texts screened but not included (n=74)

First Author	Year	PMID	Reason for exclusion
Yamada	1989	2508310	No HER2 data
Kernohan	1991	1672154	No quantitative SGC HER2 IHC or ISH data
Shrestha	1992	1361005	No quantitative SGC HER2 IHC or ISH data
Sugano	1992	1353853	“Unique” scoring system of HER2 IHC
Delgado	1993	7688652	No quantitative SGC HER2 IHC or ISH data
Hellquist	1994	7931825	No quantitative SGC HER2 IHC or ISH data
Kärjä	1994	7915830	No quantitative SGC HER2 IHC or ISH data
Müller	1994	7991521	No quantitative SGC HER2 IHC or ISH data
Press	1994	7522962	No quantitative SGC HER2 IHC or ISH data
Cho	1995	7726139	No quantitative SGC HER2 IHC or ISH data
Giannoni	1995	7870438	No quantitative SGC HER2 IHC or ISH data
Shintani	1995	8669836	No quantitative SGC HER2 IHC or ISH data
Felix	1996	8666365	No quantitative SGC HER2 IHC or ISH data
Kamio	1996	8925128	No quantitative SGC HER2 IHC or ISH data
Rosa	1996	8729044	No quantitative SGC HER2 IHC or ISH data
Cho	1997	9443087	Case report and no quantitative SGC HER2 IHC or ISH data

Martinez-Barba	1997	8625227	(Listed as review) No quantitative SGC HER2 IHC or ISH data
Suzuki	1998	10211217	No quantitative SGC HER2 IHC or ISH data
Wick	1998	9426521	No quantitative SGC HER2 IHC or ISH data
Cho	1999	10402521	No quantitative SGC HER2 IHC or ISH data
Jaehne	2001	11555785	Article in German
Gibbons	2001	11568571	No quantitative SGC HER2 IHC or ISH data
Lewis	2001	11431714	No quantitative SGC HER2 IHC or ISH data
O'Malley	2001	11293897	Study on breast cancer, no SGC HER2 IHC or ISH data
Haddad	2003	12907212	Preselected patient population
Nguyen	2003	14974865	Not accessible
Nagler	2003	12759537	No prevalence data
Etges	2003	14645349	No quantitative SGC HER2 IHC or ISH data
Simpson	2003	12883239	Case report
Brandwein-Gensler	2004	15252310	Case report and no definition of HER2
Dagrada	2004	14987238	Article is a case report / "comment"
Nagao	2004	15323139	Case report
Freitas	2005	16273189	No quantitative SGC HER2 IHC or ISH data

Locati	2005	7991521	Article is a “Comment”
Laurie	2006	16763282	Review
Sørensen	2006	16630292	No data on HER2
Agulnik	2007	17761983	Study on pre-selected population
Ihrler	2007	17593217	No data on HER2
Matsubayashi	2007	17310348	No quantitative IHC or ISH HER2 data
Sasaki	2007	17192791	No data on HER2 status in SGC
Johnson	2008	18091319	Not accessible
Ettl	2008	18214402	Article in German
Nashed	2009	18405406	Case report
Vidal	2009	19309723	Study on pre-selected population
Lujan	2010	20664595	No HER2 data
Hashimoto	2011	21317706	Data already included in Hashimoto 2012
Santini	2012	24006824	Article in French
Ettl	2012	22240798	No discrimination between histological subtype and HER2 status
Golusinski	2013	24021827	Article in Polish
Jayaprakash	2014	23606370	No HER2 data

Limaye	2013	23429737	Study on pre-selected population
Ettl	2013	23780687	No discrimination between histological subtype and HER2 status
Kuo	2013	23821212	Review
Otsuka	2013	24191589	Article in Japanese
Perissinotti	2013	23749912	Study on pre-selected population
Simpson	2013	23821208	Review
Stenman	2013	23821214	Review
Yamamoto	2014	25087467	Case Report
Grünewald	2015	26053092	No IHC or ISH HER2 data
Huo	2015	26575266	No SGC data
Masubuchi	2015	24553861	Does not discriminate between SGC subtypes
Dalin	2016	27103403	No extractable HER2 IHC data
Gilbert	2016	26939990	Study not clear HER2 positivity criteria
Wang	2016	27334835	No quantitative SGC HER2 IHC or ISH data
Krings	2017	28548128	HER2 status not performed
Schmitt	2017	29103750	Review
Shams	2018	N/A	Article not accessible
Takahashi	2018	30452336	Study on pre-selected population

Kurzrock	2019	32067683	Study on pre-selected population
Stodulski	2019	31062093	No definition of HER2 positivity
Hanna	2020	32310325	No discrimination between histological subtype and HER2 status

S4: Salivary Duct Carcinoma overall and IHC assay subgroup analysis

Salivary duct carcinoma: Overall			
Assay	Number of studies	Prevalence Estimate	95% CI
DAKO	19	46.4340	31.7966; 61.7127
Labvision	1	15.1515	8.3507; 25.9243
Neomarkers	1	27.1186	17.3278; 39.7797
No IHC done	1	42.1053	22.6327; 64.3884
Roche	3	46.1538	20.5701; 73.9378
Unknown	1	39.2857	23.2592; 58.0079
Ventana	11	44.1469	35.6145; 53.0397
Test for subgroup differences (random effects model): p-value: 0.0017			

Salivary Duct Carcinoma: IHC 0			
Assay	Number of studies	Prevalence Estimate	95% CI
Ventana	8	25.1282	18.5098; 33.1504
DAKO	8	32.6954	11.0481; 65.5170
Neomarkers	1	26.1905	17.9097; 36.5933
Labvision	1	74.2424	62.4083; 83.3453
Test for subgroup differences (random effects model): p-value < 0.0001			

Salivary Duct Carcinoma: IHC 1+			
Assay	Number of studies	Prevalence Estimate	95% CI
Ventana	8	14.0028	7.5018; 24.6370
DAKO	8	5.4824	1.6132; 17.0252
Neomarkers	1	19.0476	12.0097; 28.8573
Labvision	1	6.0606	2.2934; 15.0620
Test for subgroup differences (random effects model): p-value 0.0361			

Salivary Duct Carcinoma: IHC2+			
Assay	Number of studies	Prevalence Estimate	95% CI
Ventana	8	18.9744	13.1982; 26.5064
DAKO	8	7.7966	1.9964; 25.9814
Neomarkers	1	29.7619	20.9757; 40.3492
Labvision	1	4.5455	1.4734; 13.1666
Test for subgroup differences (random effects model): p-value 0.0011			

Salivary Duct Carcinoma: IHC3+			
Assay	Number of studies	Prevalence Estimate	95% CI
Ventana	8	40.5947	30.8457; 51.1461
DAKO	8	41.4235	21.1502; 65.0884
Neomarkers	1	25.0000	16.9036; 35.3258
Labvision	1	15.1515	8.3507; 25.9243
Test for subgroup differences (random effects model): p-value 0.0017			

S5: Tissue types with low number of observations.

Squamous Cell Carcinoma

Study	HER2 definition	Events	Total	HER2 Positivity (%)	Events	95%-CI
Tapia 2007	IHC2 and ISH or IHC3	0	2		0.00	[0.00; 65.76]
Glisson 2004	IHC2 or IHC3	3	5		60.00	[23.07; 88.24]
Hashimoto 2017	IHC2 and ISH or IHC3	1	5		20.00	[3.62; 62.45]
Ettl 2008	IHC2 or IHC3	2	5		40.00	[11.76; 76.93]
Ettl 2012	IHC3	1	22		4.55	[0.81; 21.80]

Epithelial-myoepithelial carcinoma

Study	HER2 definition	Events	Total	HER2 Positivity (%)	Events	95%-CI
Hashimoto 2017	IHC2 and ISH or IHC3	0	5		0.00	[0.00; 43.45]
Clauditz 2011	IHC3 or ISH	1	51		1.96	[0.35; 10.30]

Poorly differentiated carcinoma

Study	HER2 definition	Events	Total	HER2 Positivity (%)	Events	95%-CI
Locati 2015	IHC2 and ISH or IHC3	0	1		0.00	[0.00; 79.35]
Skálová 2001	IHC2 or IHC3	0	3		0.00	[0.00; 56.15]
Locati 2009	IHC2 and ISH or IHC3	1	4		25.00	[4.56; 69.94]
Hashimoto 2017	IHC2 and ISH or IHC3	0	7		0.00	[0.00; 35.43]

Polymorphus adenocarcinoma

Study	HER2 definition	Events	Total	HER2 Positivity (%)	Events	95%-CI
Hashimoto 2017	IHC2 and ISH or IHC3	0	3		0.00	[0.00; 56.15]
Ettl 2012	IHC3	0	11		0.00	[0.00; 25.88]
Clauditz 2011	IHC3 or ISH	0	36		0.00	[0.00; 9.64]

Basal Cell Carcinoma

Study	HER2 definition	Events	Total	HER2 Positivity (%)	Events	95%-CI
Skálová 2001	IHC2 or IHC3	0	1		0.00	[0.00; 79.35]
Suzuki 2012	IHC2 or IHC3	0	2		0.00	[0.00; 65.76]
Hashimoto 2017	IHC2 and ISH or IHC3	0	3		0.00	[0.00; 56.15]
Ettl 2008	IHC2 or IHC3	0	3		0.00	[0.00; 56.15]
Clauditz 2011	IHC3 or ISH	0	24		0.00	[0.00; 13.80]

Oncocytic Carcinoma

Study	HER2 definition	Events	Total	HER2 Positivity (%)	Events	95%-CI
Hashimoto 2017	IHC2 and ISH or IHC3	0	1		0.00	[0.00; 79.35]
Ettl 2008	IHC2 or IHC3	0	1		0.00	[0.00; 79.35]
Clauditz 2011	IHC3 or ISH	0	12		0.00	[0.00; 24.25]

Hashimoto 2017 reported one patient with clear cell carcinoma with no HER2 positivity defined as IHC2+ and ISH amplification or IHC3+.

Suzuki 2012 and Ettl 2008 reported a total of five patients with lymphoepithelial carcinoma of which zero were HER2 positive.

Hsieh 2020 reported on nine patients of Intraductal Carcinoma in which one was IHC2+.