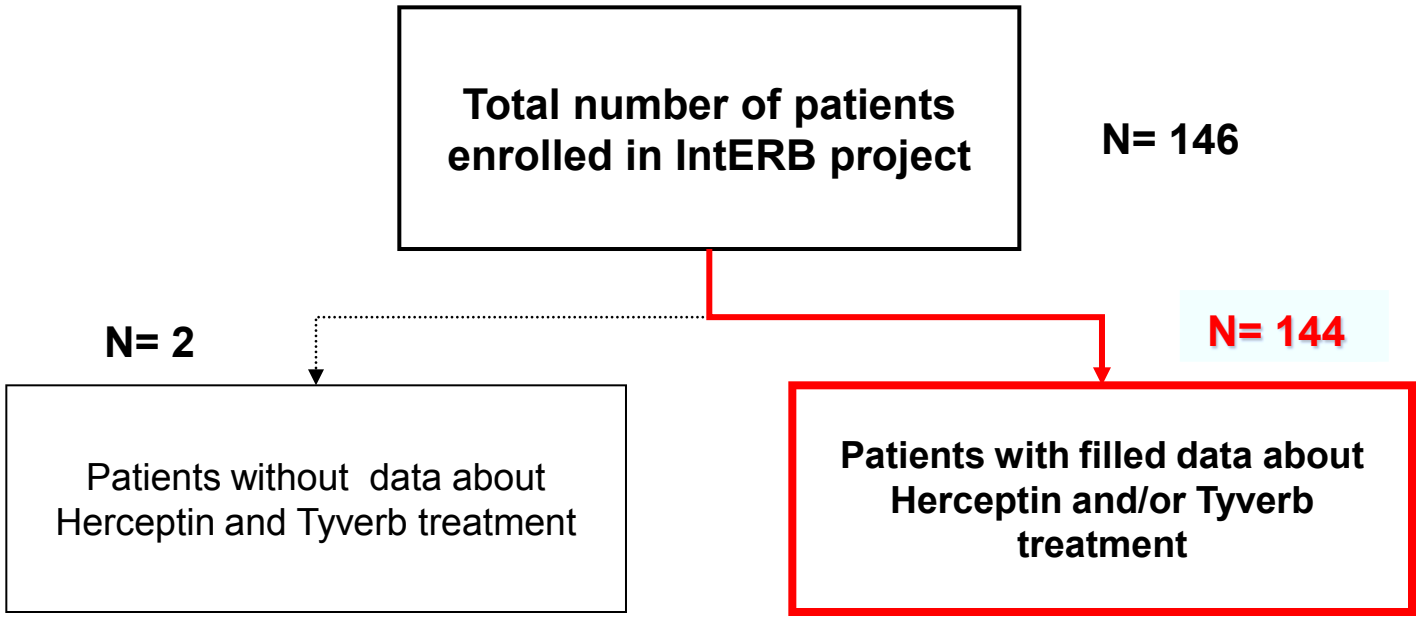
Project intERB overview

Project intERB was initiated in 2008 with the aim to describe epidemiology and treatment management of ERBB positive breast cancer patients with treatment targeting ERBB receptor. The idea was to introduce the project in all countries of CE region. However, only centres from the Czech Republic, Hungary and Lithuania decided to participate actively. Czech intERB (Herceptine/Lapatinib) registry became a part of the larger project Breast in 2011. The Breast project monitors all patients treated with various treatments reserved for tertiary referral centres (comprehensive cancer care centres). The structure of the database was modified in 2011 to accommodate the new needs.

The original Database intERB was used by centres from Hungary and Lithuania until the official end of the project 31. 12. 2012.

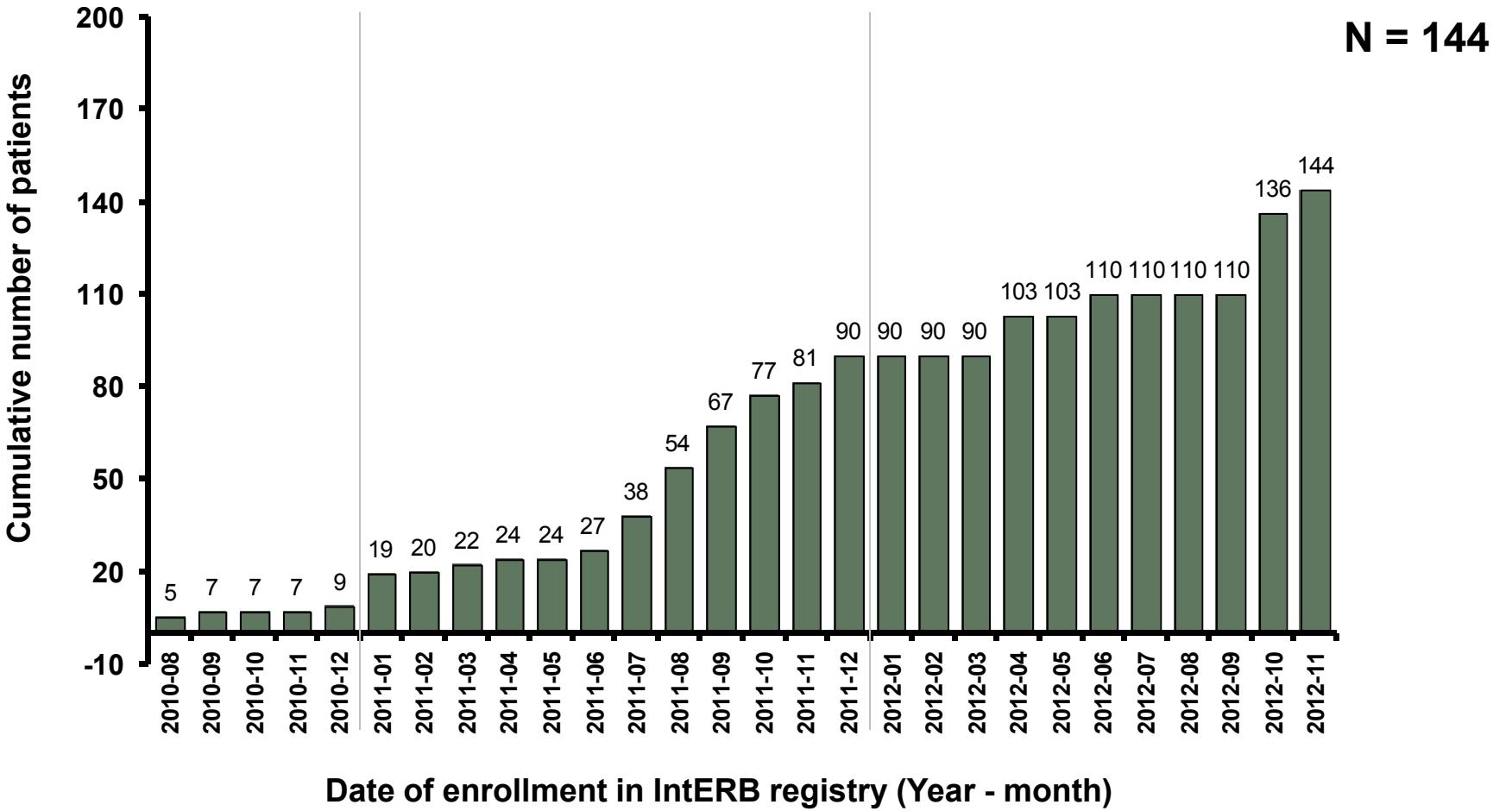
Number of patients in IntERB project



Number of patients in IntERB project

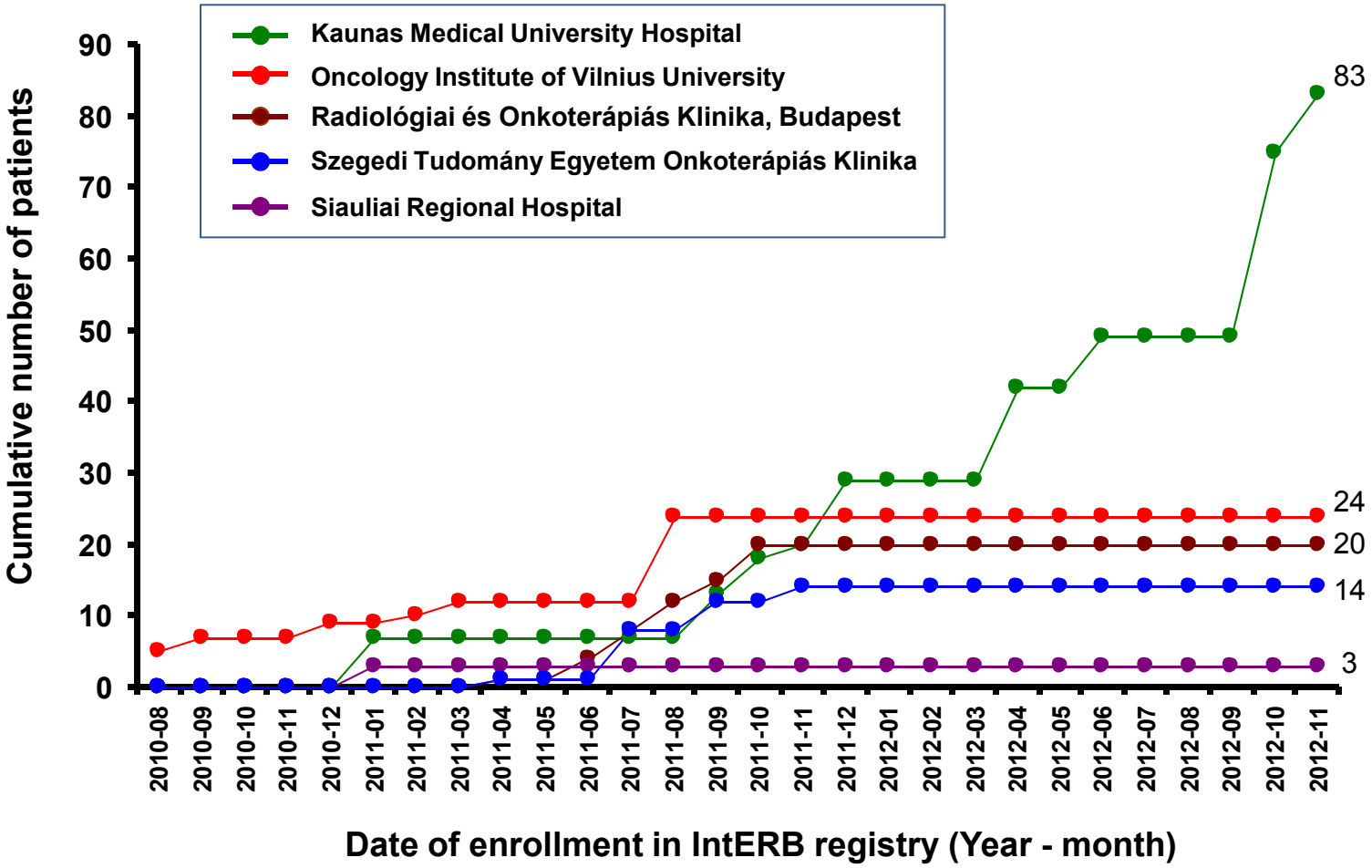
Hospital	Total number of patients		Total number of patients with filled data about Herceptin and/or Tyverb treatment	
	N	%	N	%
Kaunas Medical University Hospital	83	56.8	83	57.6
Oncology Institute of Vilnius University	24	16.4	24	16.7
Radiológiai és Onkoterápiás Klinika, Budapest	20	13.7	20	13.9
Szegedi Tudomány Egyetem Onkoterápiás Klinika	15	10.3	14	9.7
Siauliai Regional Hospital	4	2.7	3	2.1
Total	**146**	**100.0**	**144**	**100.0**

Date of enrollment in IntERB registry



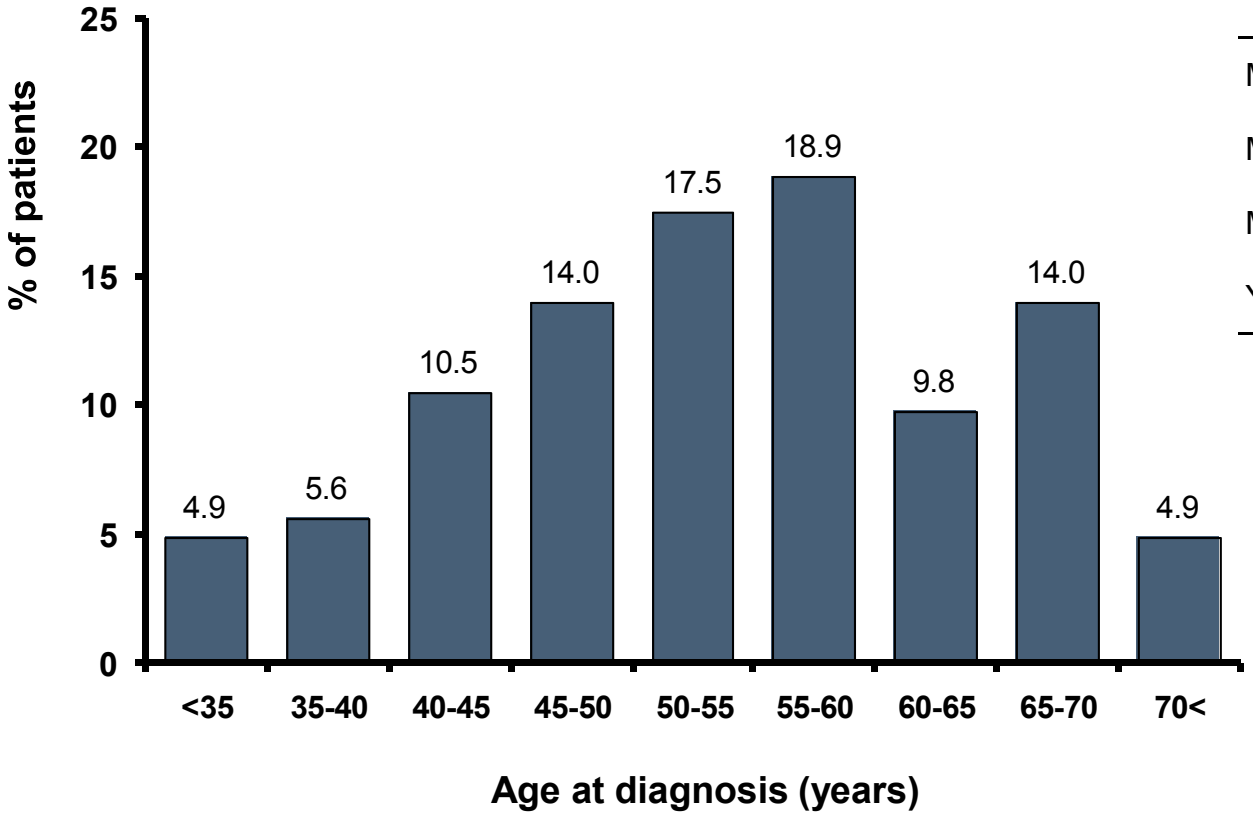
Date of enrollment in IntERB registry - according to hospital

N = 144



Primary diagnosis

Age at diagnosis



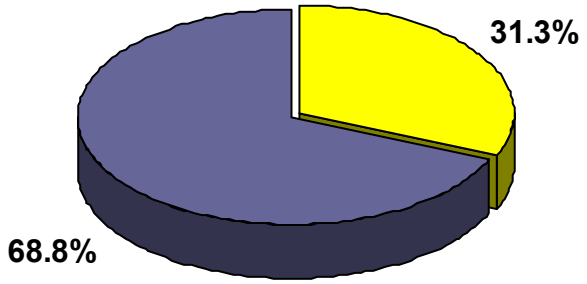
N = 144

Mean	54 years
Median	55 years
Min – Max	32 - 80 years
Younger than 65 yrs	91 (81.1%)

Affected side and ovarian function at the time of diagnosis

Ovarian function at the time of diagnosis

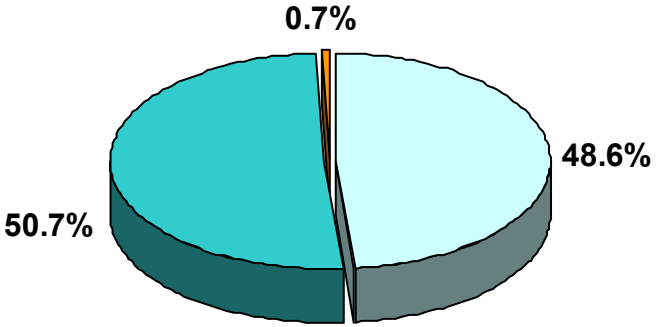
N = 144



Pre menopause
(N = 45)

Post menopause
(N = 99)

Affected side



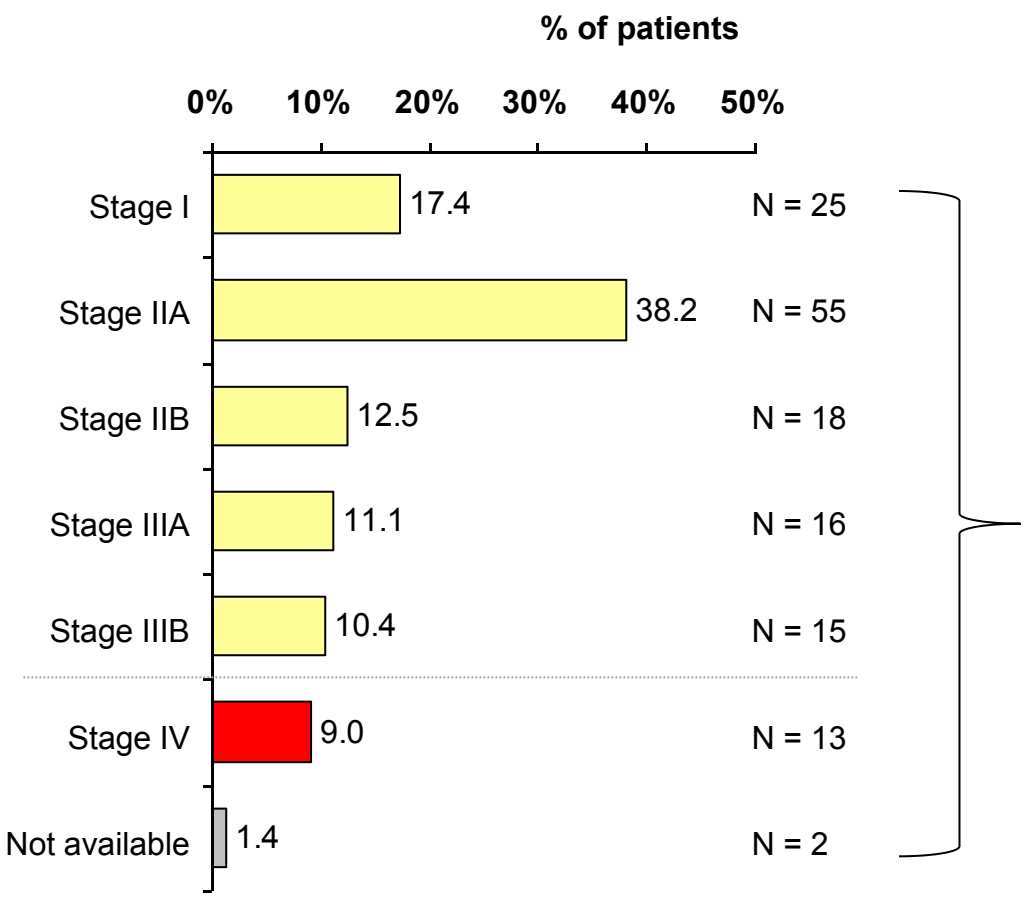
Right
(N = 70)

Left
(N = 73)

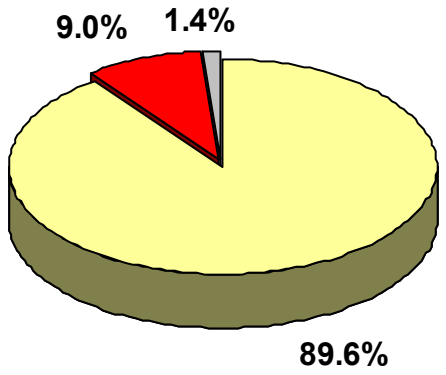
Bilateral
(N = 1)

Stage of the primary tumour

N = 144



Extent of the disease at diagnosis



Non metastic disease
(N = 129)

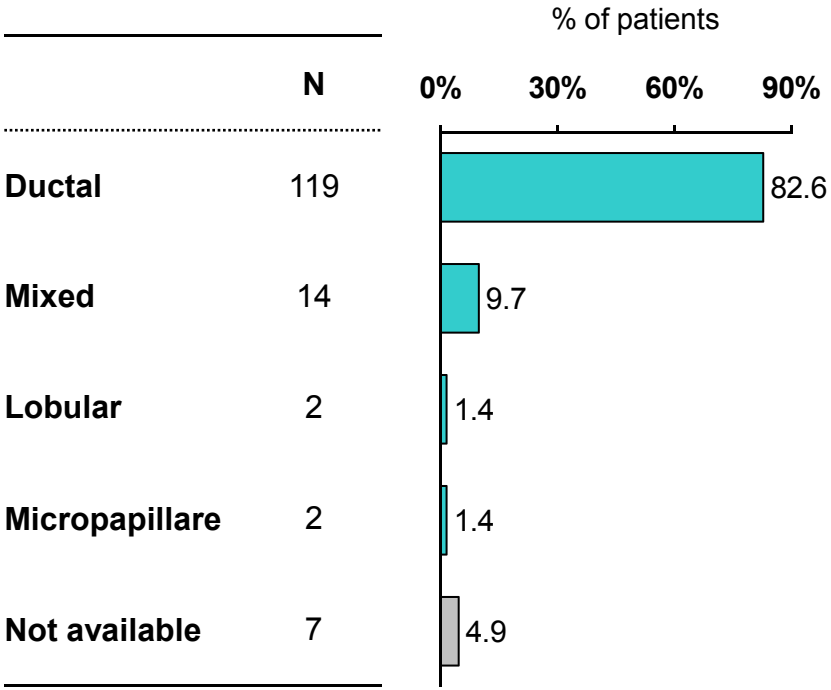
Metastic disease
(N = 13)

Metastic disease
(N = 2)

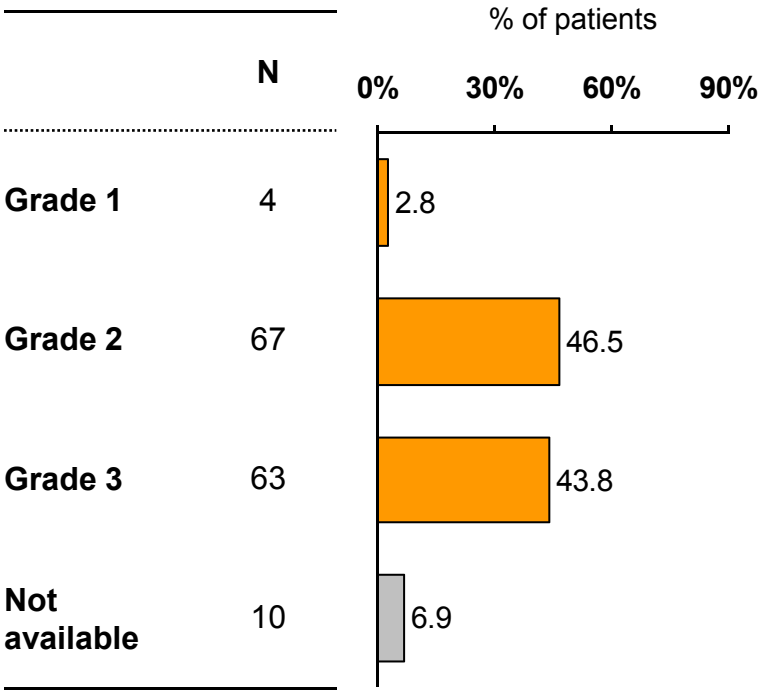
Histological type and grade of primary tumour

Histological type

N = 144



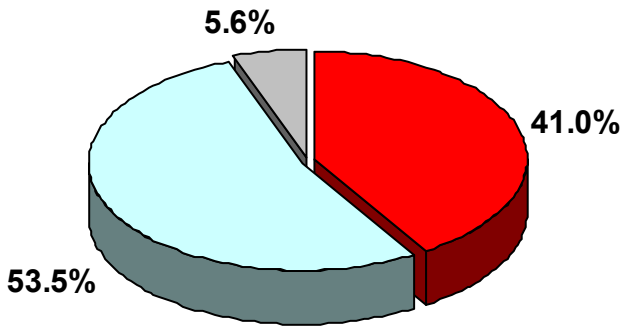
Grade



Estrogen and progesterone receptor

Estrogen receptors

N = 144

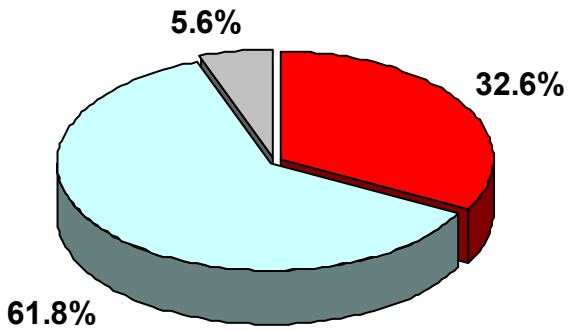


Positive
(N = 59)

Negative
(N = 77)

Not available
(N = 8)

Progesterone receptors



Positive
(N = 47)

Negative
(N = 89)

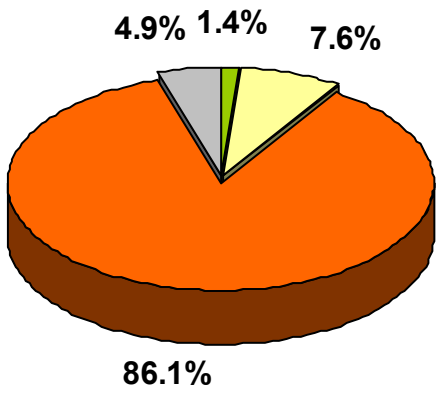
Not available
(N = 8)

Her-2/neu examination

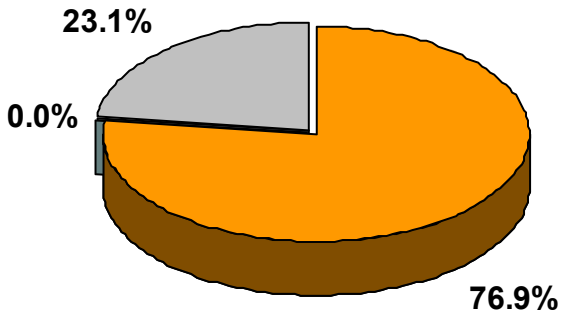
HER-2/neu - immunohistochemical

HER-2/neu - in situ hybridization

N = 144



N = 13 with IHC 1+ or 2+



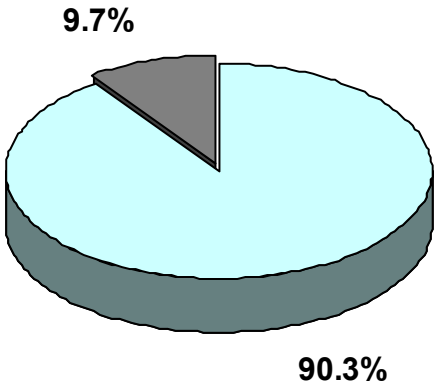
- **1+** (N = 2)
- **2+** (N = 11)
- **3+** (N = 124)
- **Not available** (N = 7)

- **Positive** (N = 10)
- **Negative** (N = 0)
- **Not available** (N = 3)

Surgery before ERB2 targeted therapy

Surgery

N = 144

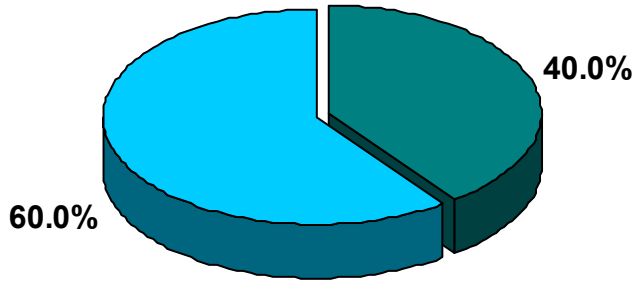


Yes (N = 130)

No (N = 14)

Extent of surgery

N = 130



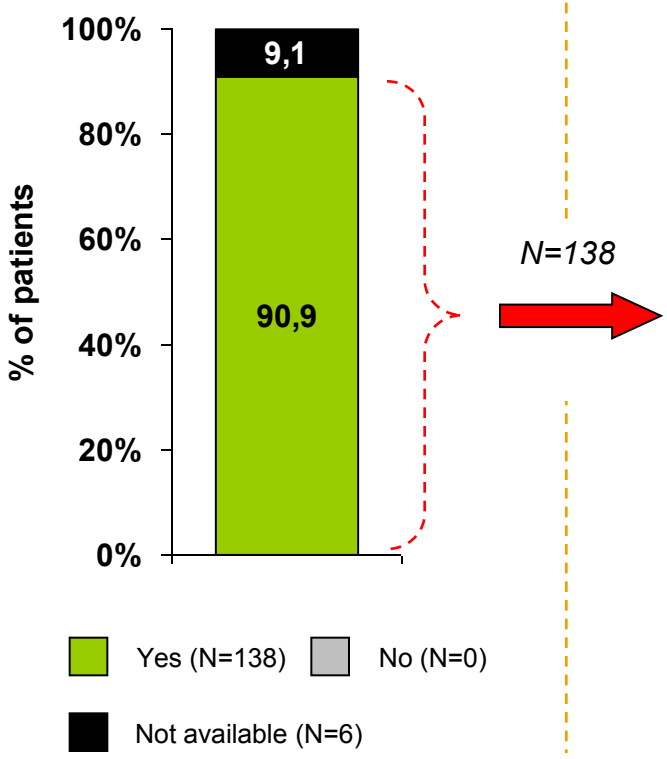
Radical (Mastectomy)
(N = 52)

Conservative surgery (Lumpectomy, Quandrantectomy)
(N = 78)

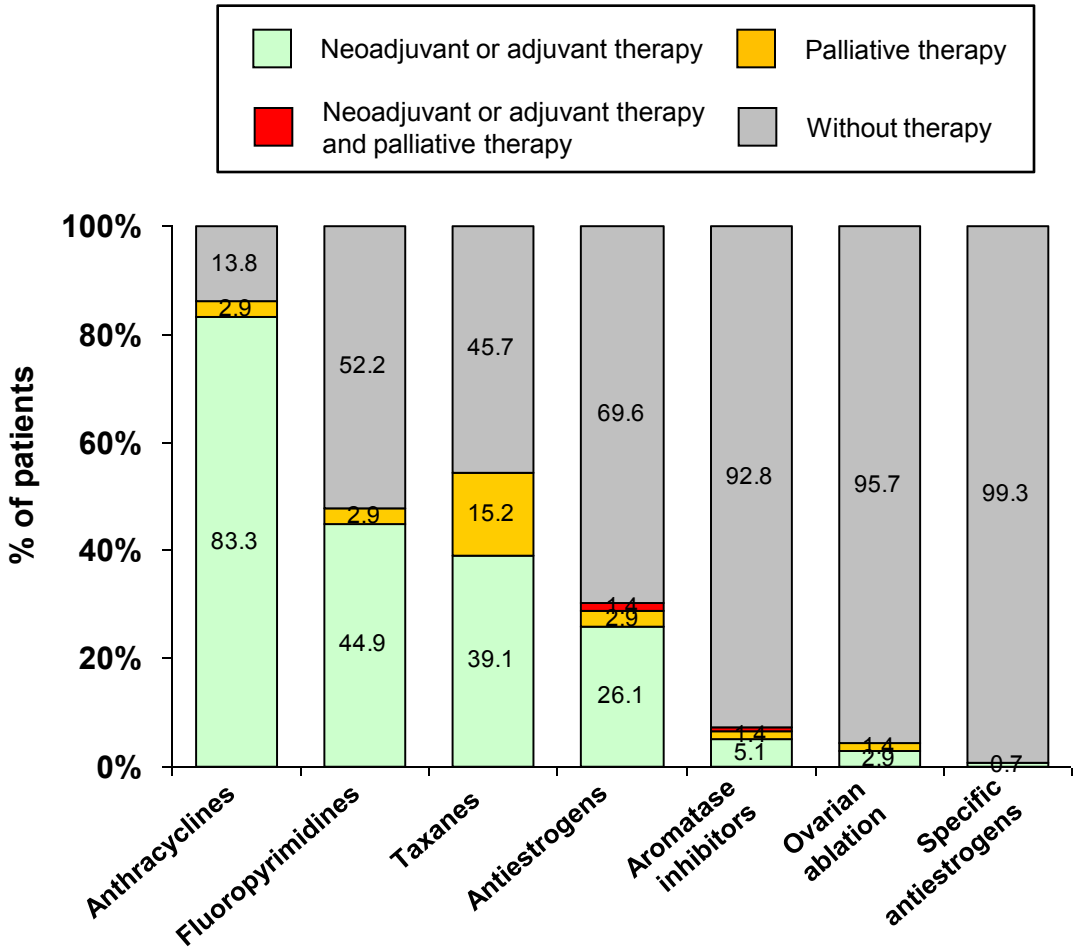
Summary of non ERB2 targeted therapy

Has the patient undergone any cytostatic therapy (non ERB2 targeted CHT, HT)

N = 144



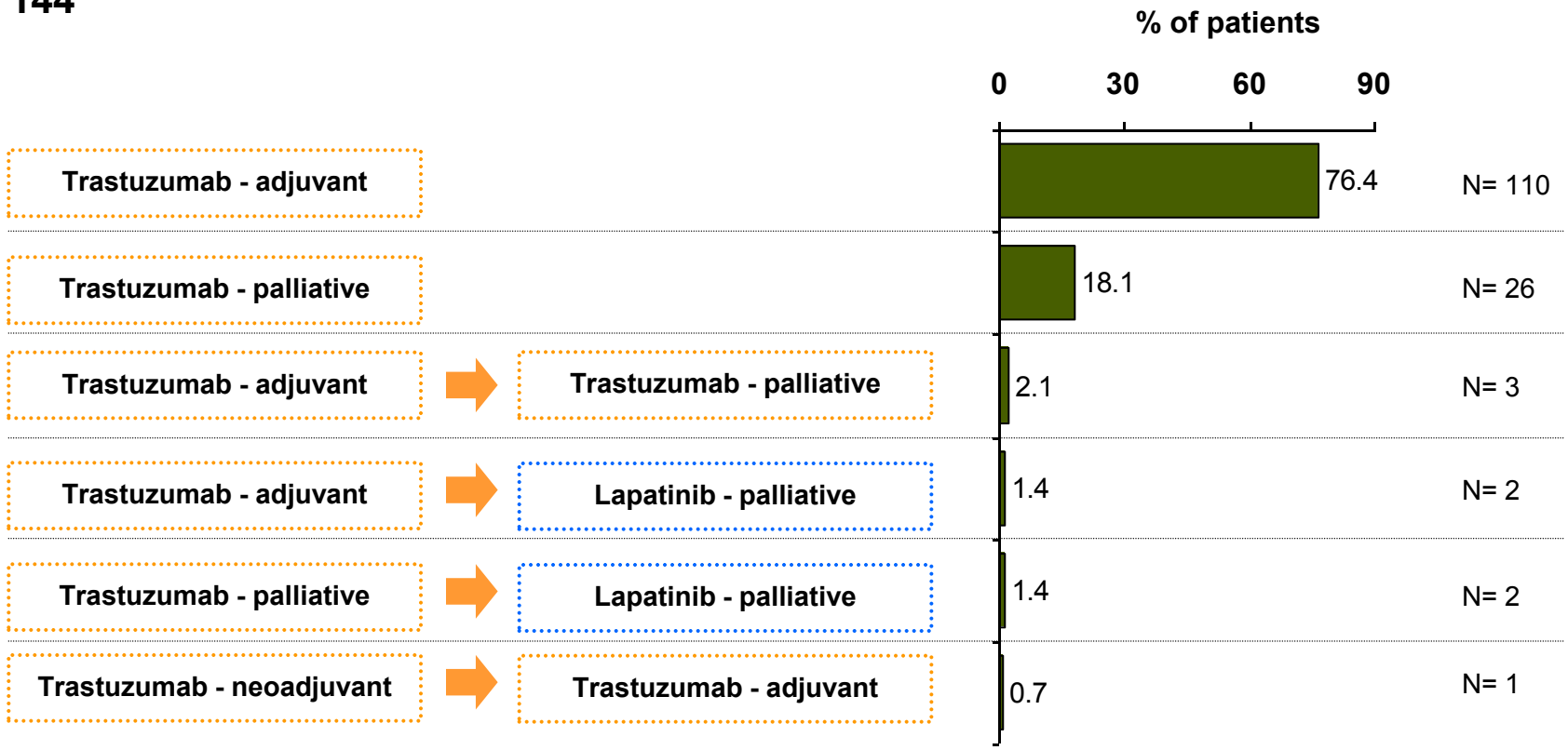
N=138



ERB2 targeted therapy

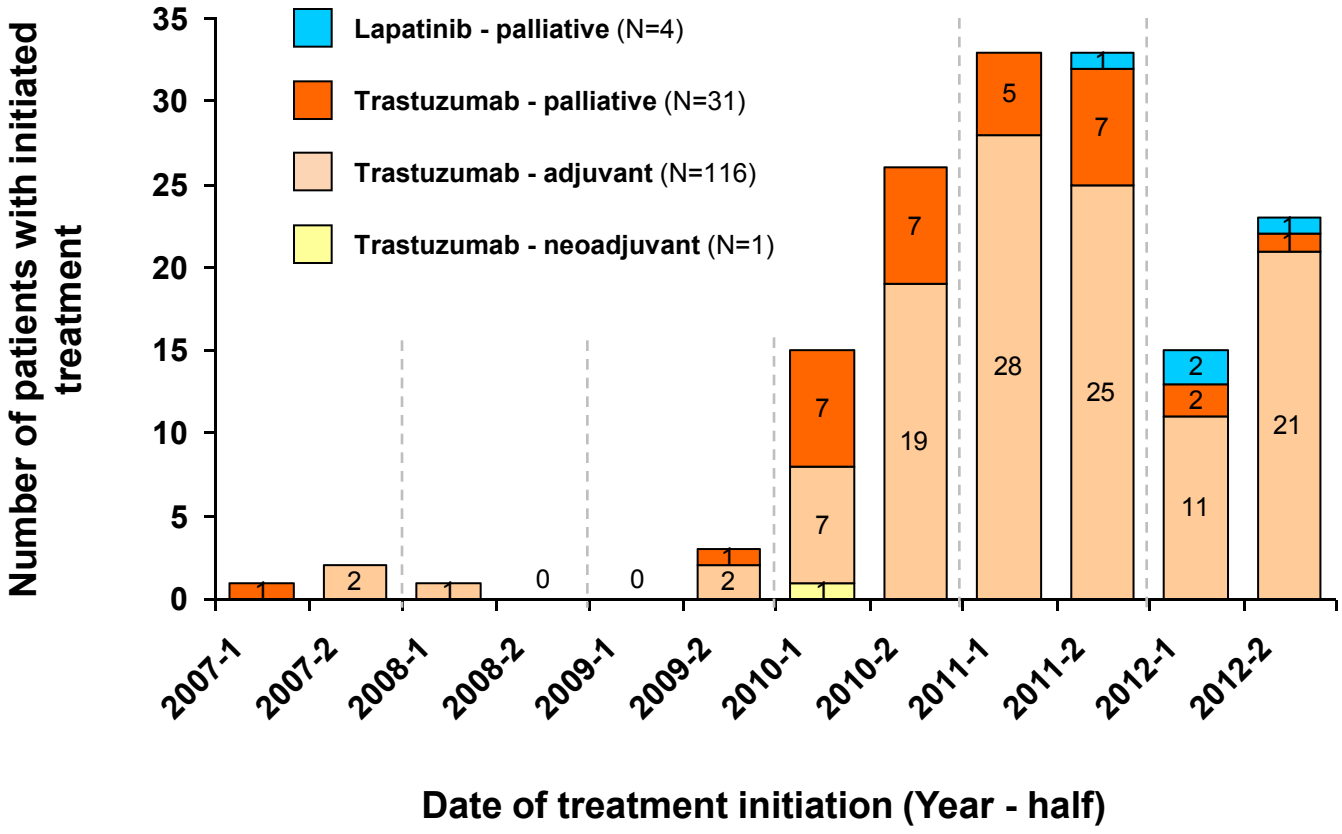
Sequence of ERB2 targeted therapy

N = 144



Year of treatment initiation

N = 144

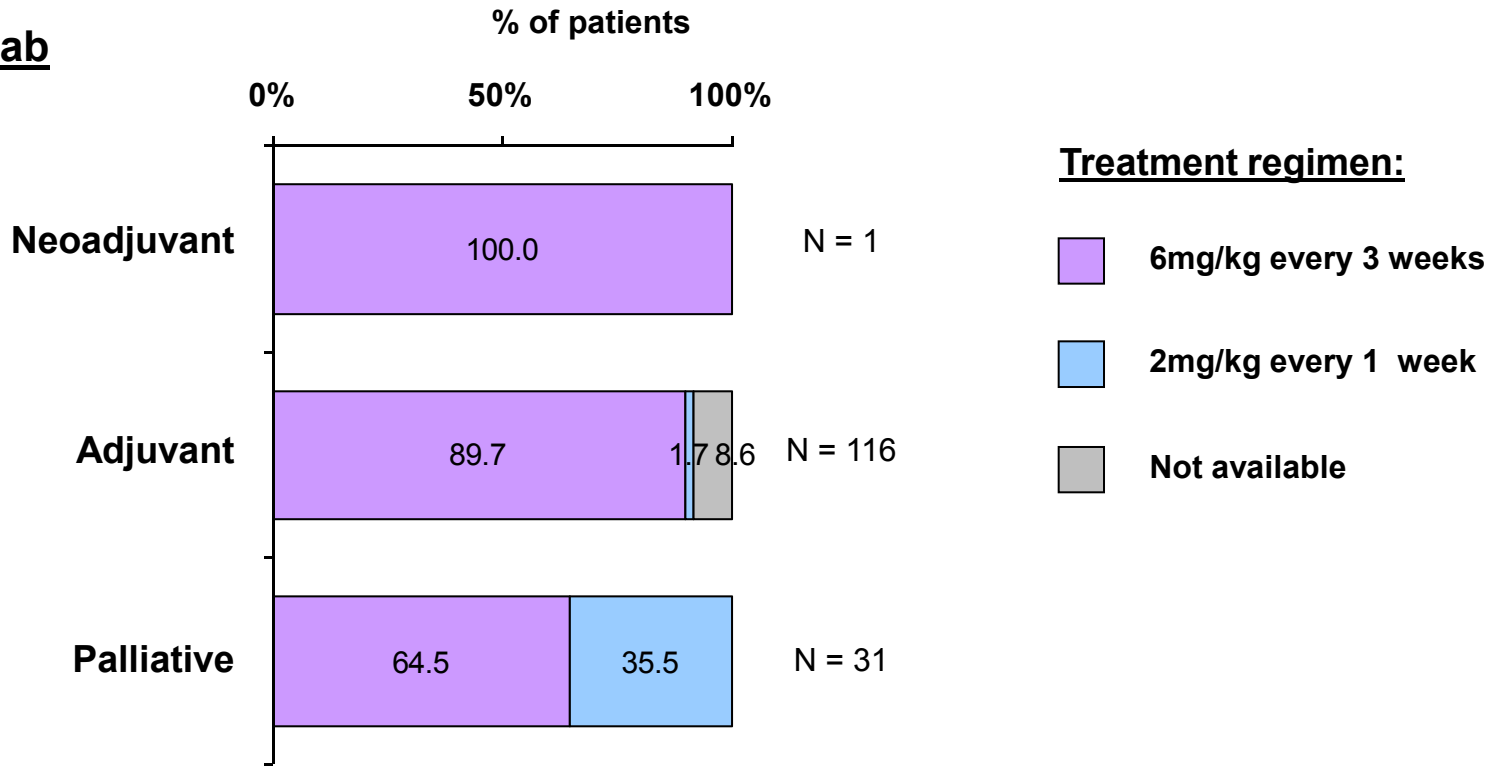


Patients treated with trastuzumab

Trastuzumab treatment regimen

N = 144

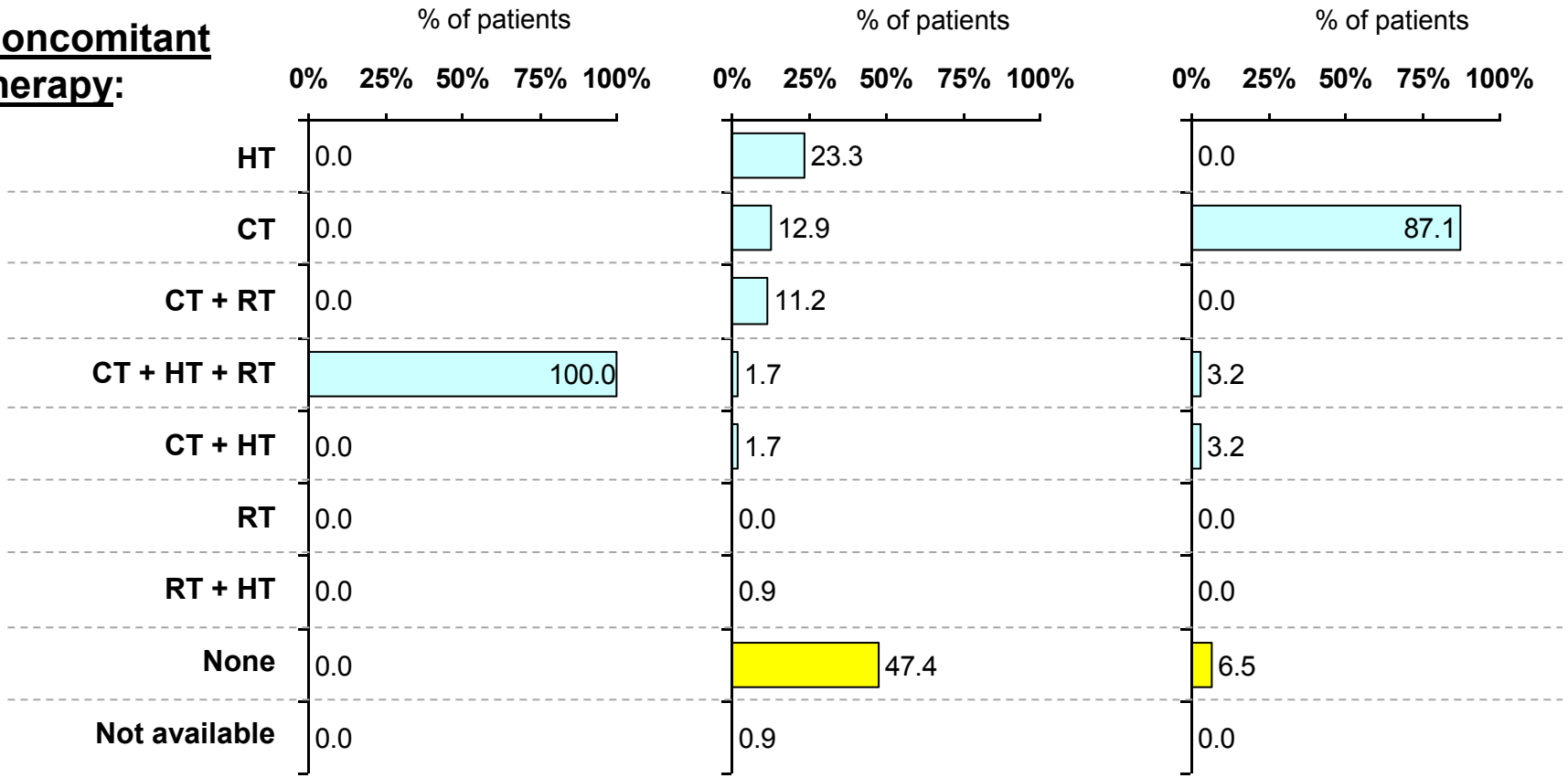
Trastuzumab indication:



Concomitant therapy during trastuzumab treatment

N = 144

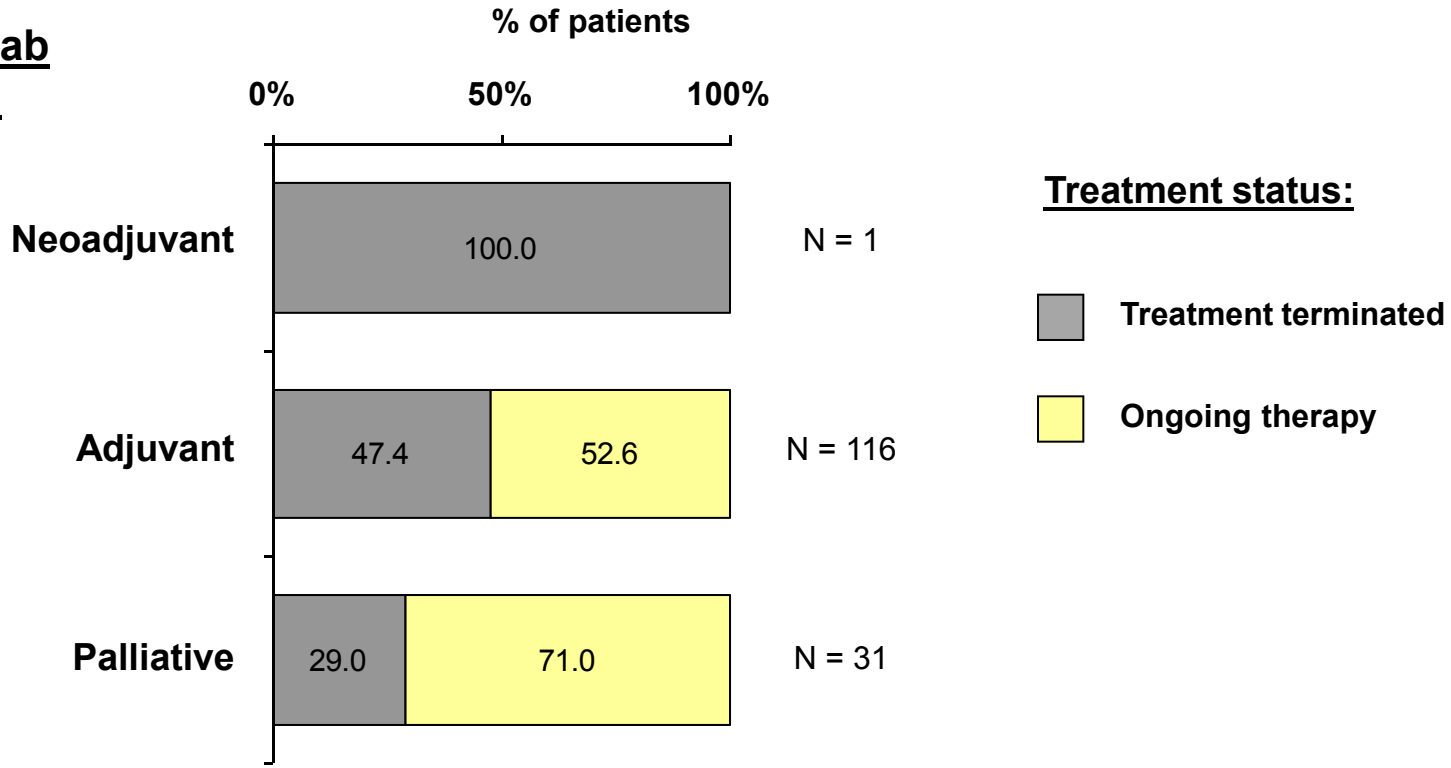
Concomitant therapy:



Trastuzumab treatment status as of last update

N = 144

Trastuzumab indication:



The median adjuvant trastuzumab treatment duration (N= 55) is 11.6 months (mean 11,2 months).
The median palliative trastuzumab treatment duration (N=9) is 11.9 months (mean 12.2 months).

Adverse events during trastuzumab treatment

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6	Patient 7
Trastuzumab indication	Adjuvant	Adjuvant	Adjuvant	Adjuvant	Adjuvant	Palliative	Palliative
Time to AE from trastuzumab treatment initiation	0.7 months	2.8 months	9.2 months	3.5 months	3.0 months	13.6 months	1.7 monhts
Type of AE	Lower extremity numbness and joint pain	Artralgia, myalgia	Chest pain	Decrease of EF - Cardiotoxicity	Fluctuation in blood pressure	Arthralgia, myalgia	Urinary tract infection
Relatedness of adverse event to trastuzumab treatment	undetectable	improbable	probable	probable	undetectable	probable	improbable
Was it serious adverse event?	No	No	No	No	No	No	Patient admitted to hospital / hospital stay extended

In general there is under-reporting of adverse events across all projects without direct control of source data by specialized monitors

Patients treated with lapatinib

Patients treated with lapatinib - part 1

		Patient 1	Patient 2	Patient 3	Patient 4
Primary diagnosis	**Age at diagnosis**	69 years	55 years	47 years	39 years
	TNM of primary tumour	T1N0M0	T1N0M0	T1N0M0	T1N0M1
	Ovarian function at the time of diagnosis	Post menopause	Post menopause	Post menopause	Pre menopause
	Affected side	Left	Right	Left	Left
	Histological type	Ductal	Ductal	Ductal	Ductal
	Grade	2	2	2	3
	Estrogen receptor	Negative	Positive	Negative	Negative
	Progesterone receptor	Negative	Negative	Negative	Negative
Preceding therapy	**Surgery (extent)**	Yes (Radical)	Yes (Radical)	Yes (Conservative)	Yes (Conservative)
	Radiotherapy	No	No	Yes	No
	Anthracyklines	Yes	Yes	Yes	No
	Fluoropyrimidines	No	No	Yes	No
	Taxanes	Yes	No	No	Yes
	Antiestrogens	No	No	No	No
	Aromatase inhibitors	No	No	No	No
	Ovarian ablation	No	No	No	No
	Trastuzumab	palliative	adjuvant	adjuvant	palliative

Patients treated with lapatinib - part 2

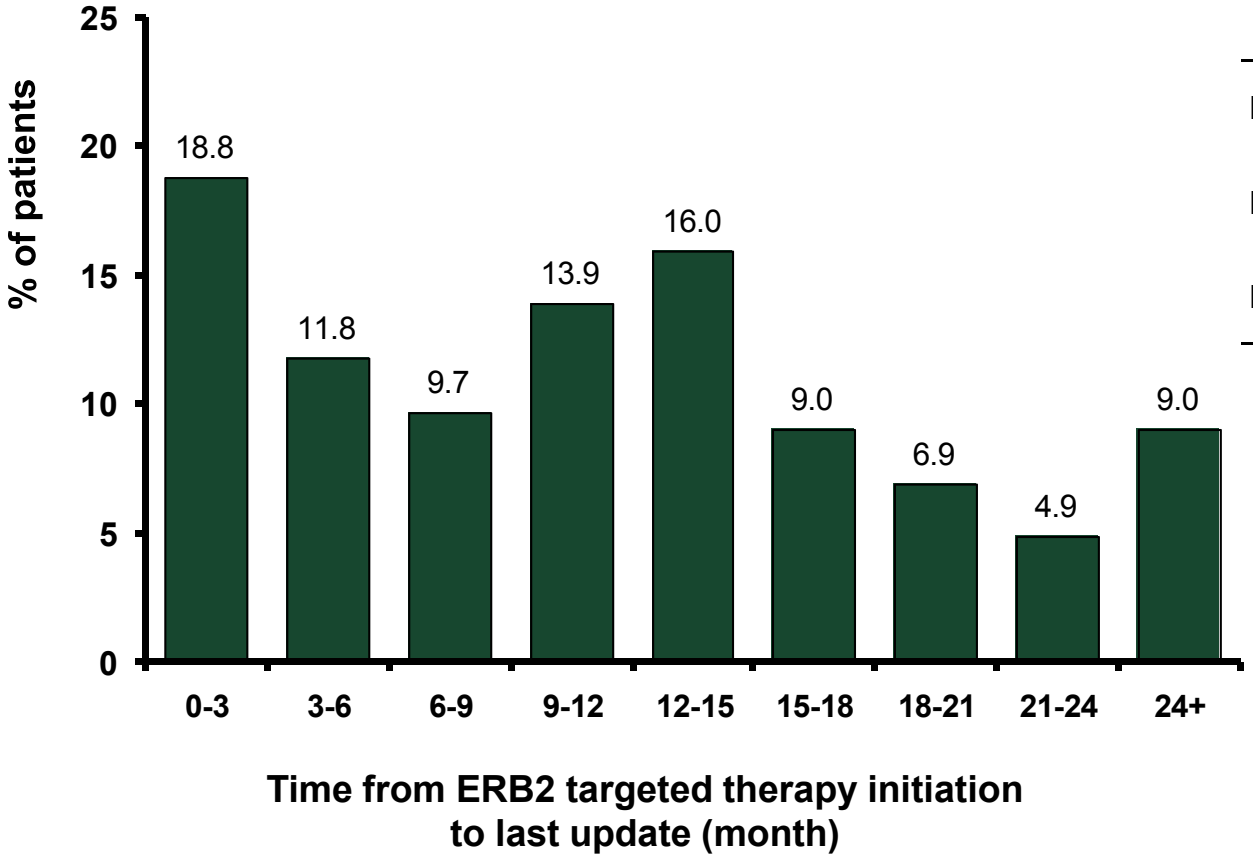
		Patient 1	Patient 2	Patient 3	Patient 4
Lapatinib treatment	**Age at treatment initiation**	71 years	56 years	49 years	41 years
	Stage at treatment initiation	IV	IV	IV	IV
	Line of treatment	2nd line	2nd line	1st line	2nd line
	Metastases	Lung, Bone	Lung, Bone	Bone	Lung
	Daily dose	1250 mg	1250 mg	1250 mg	1750 mg
	Concomitant therapy	Capecitabine	Capecitabine	Capecitabine	Capecitabine
	Treatment status	Terminated	Terminated	Ongoing*	Terminated
	Reason for termination	Disease progression	Disease progression	-	Disease progression
	Treatment duration	2.4 months	8.8 months	1.3 months*	11.0 months
	The best response achieved	PD	SD	PR	SD*
Adverse effects		No	Yes	No	Yes
Time to AE from lapatinib treatment initiation		-	Not specified	-	4 days
Type of AE		-	Not specified	-	Diarhoea
Relatedness of adverse event to lapatinib treatment		-	Not specified	-	Probable
Was it serious adverse event?		-	Not specified	-	No

*** As of last update**

Time from ERB2 targeted therapy initiation to last update

As of the date of last update all patients were alive, except one patient who died 19 months after palliative trastuzumab treatment initiation.

N = 144



Mean	12.3 months
Median	11.3 months
Min – Max	0 – 52.8 months

Project Summary – general information

From 8/2010 to 11/2012 information about 144 patients (women) was collected in the database; 99 pts (68.8%) were in menopause, 45 pts (31.3%) were premenopausal women. Right and left breast were evenly affected, only in one case bilateral affection was reported. More than half of the patients (51.9%) commenced treatment in early stages (stage I + stage IIA); in 20.1% of patients the diagnosis was confirmed while the disease was already locally advanced and/or metastatic (stage IIIB and stage IV). From the histological point of view predominantly ductal type was reported (82.6%), estrogen and progesteron receptors were positive in 41% and 32.6% cases respectively. Presence of the HER2/neu receptors was mostly confirmed by immunohistochemical examination. Most patients (130 pts, 90.3%) underwent surgery prior ERBB targeted therapy; 60% underwent breast preserving operation, 40% underwent mastectomy. 106 pts (73.6%) underwent radiotherapy; 2 patients had CNS radiotherapy due to brain metastases. Anthracyclines were the most common adjuvant or neoadjuvant therapy (83.3%) (trastuzumab and ERBB targeted therapy not included) followed by fluoropyrimidines (44.9%). The most common cytostatic palliative therapy (apart from trastuzumab and ERBB targeted therapy) were taxanes (15,2%).

Trastuzumab and lapatinib

Trastuzumab 6 mg/kg every 3 weeks was predominantly used in adjuvant therapy (110 pts, 76.4%).

26 pts (18.1%) received trastuzumab as a palliative treatment, 64.5% of patients received 6 mg/kg every 3 weeks, 35.5% of patients received 2 mg/kg every week.

3 pts received trastuzumab both as an adjuvant as well as palliative treatment.

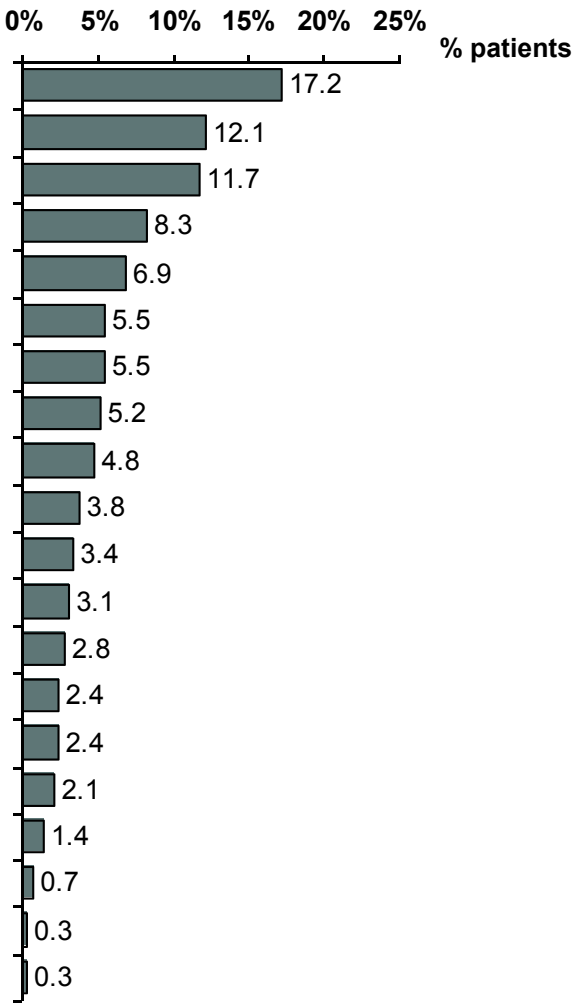
The median trastuzumab treatment duration was 11.6 months.

Slides 26 and 27 summarize lapatinib treatment of all 4 recorded patients.

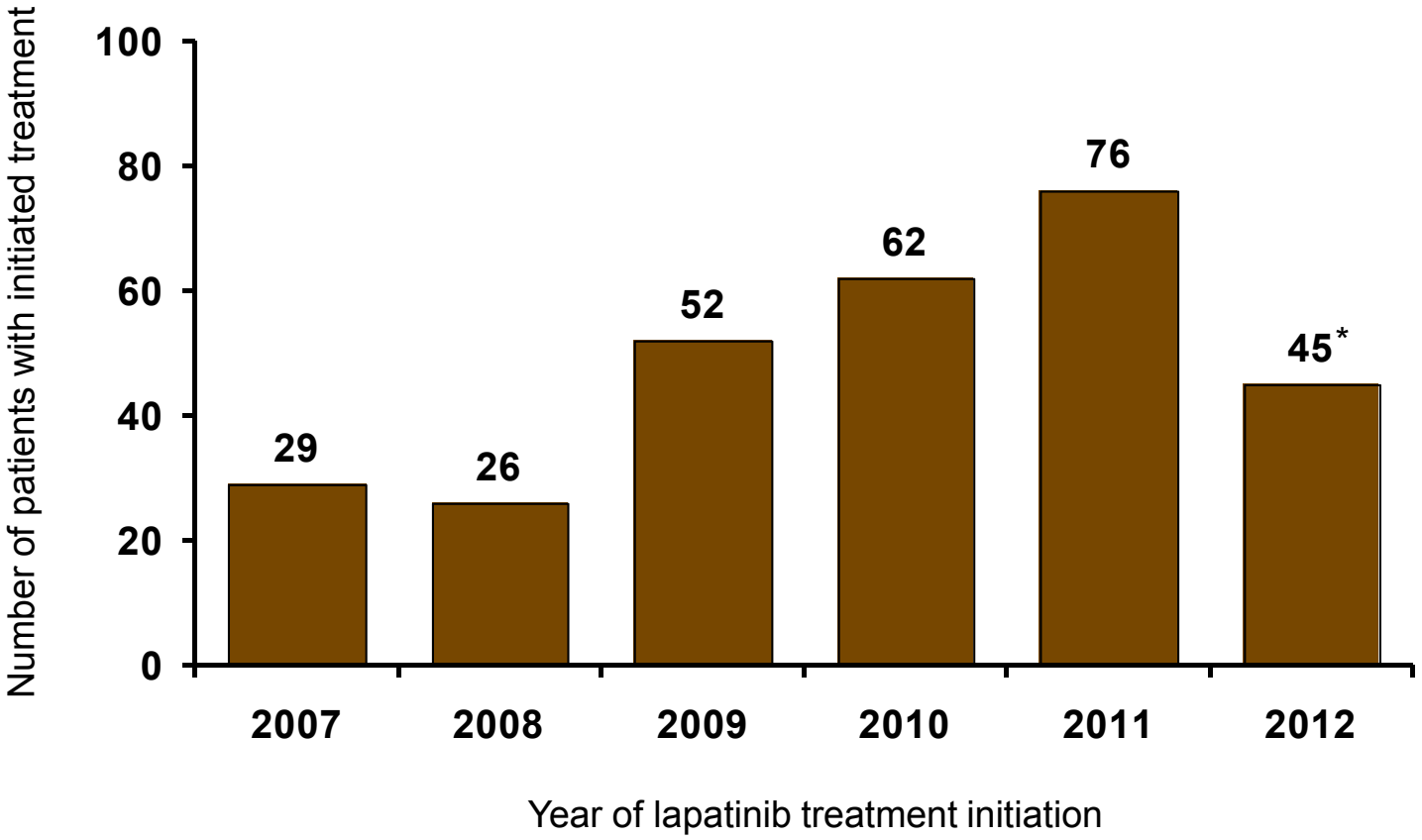
Patients treated with lapatinib in Czech Republic
-
Data from BREAST registry

Number of patients in hospitals

Hospital	N	%
MOÚ Brno	50	17.2
Všeobecná FN Praha	35	12.1
FN Olomouc	34	11.7
FN Motol, Praha	24	8.3
FN Hradec Králové	20	6.9
FN Plzeň	16	5.5
Nemocnice s poliklinikou v Novém Jičíně	16	5.5
Thomayerova nemocnice, Praha	15	5.2
Baťova nemocnice, Zlín	14	4.8
FN Brno	11	3.8
FN Ostrava-Poruba	10	3.4
Nemocnice Jihlava	9	3.1
Krajská nemocnice Liberec	8	2.8
NSPCV Chomutov	7	2.4
Masarykova nemocnice Ústí nad Labem	7	2.4
Nemocnice České Budějovice	6	2.1
Nemocnice Pardubice	4	1.4
FN u Svaté Anny v Brně	2	0.7
Nemocnice Na Bulovce, Praha	1	0.3
FN Královské Vinohrady, Praha	1	0.3
Total	**290**	**100.0**



Year of lapatinib treatment initiation



N = 290

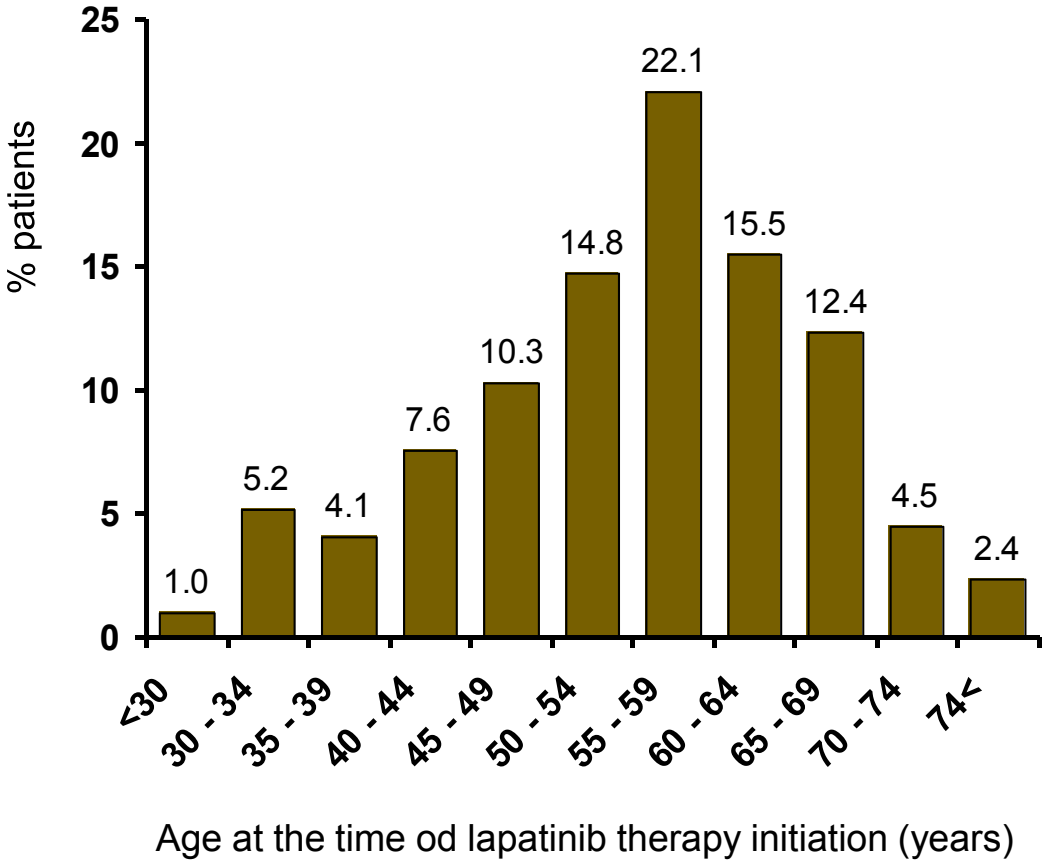
54 patients with initiated therapy till 9/2008 were involved in the EAP program.

The remaining 236 patients were not involved in the EAP programme.

*As of 8.10. 2012

Age at the time of lapatinib therapy initiation

N = 290

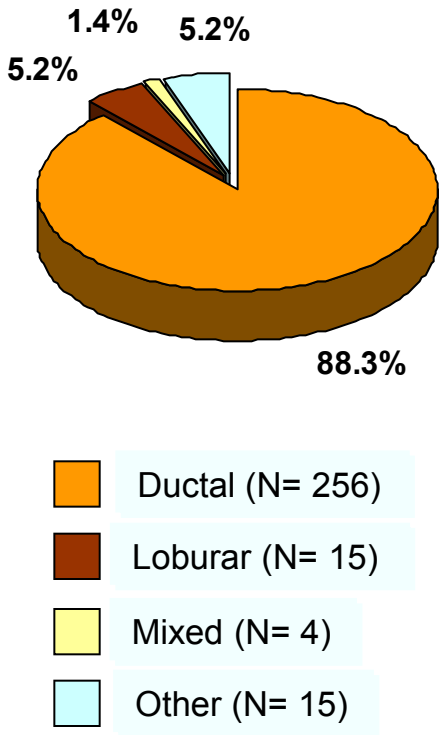


Age at the time of lapatinib therapy initiation	
N	290
Mean	55 years
Median	57 years
Min – Max	23 – 79 years

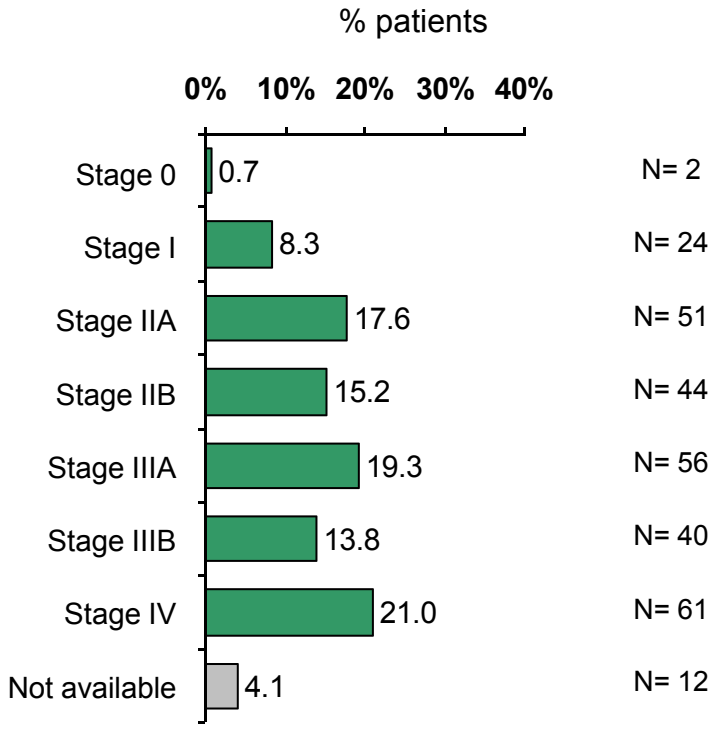
Histological type and stage of primary tumour

Histological type

N = 290



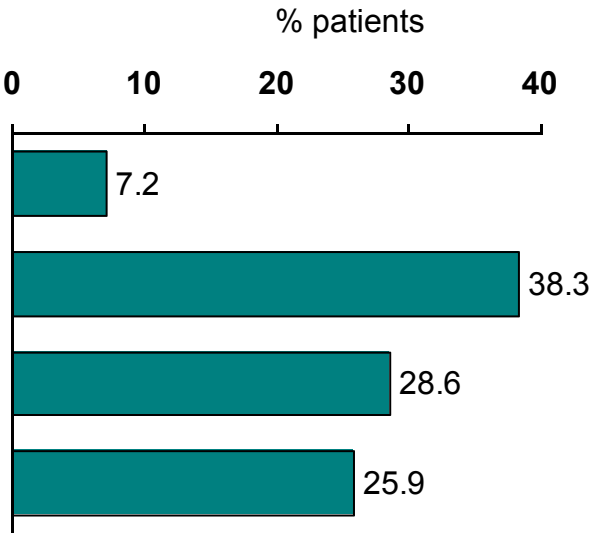
Clinical stage



Line of treatment

N = 290

Line of therapy	N	%
I. line[1)]	21	7.2
II. line	111	38.3
III. line	83	28.6
Further lines	75	25.9
Total	**290**	**100.0**



[1)] 19 patients had undergone Herceptin (neo)adjuvant therapy prior to lapatinib treatment initiated in the I. line.

Treatment modalities

Initial daily dose of lapatinib [mg]

N = 290

	N	%
750 mg	2	0.7
1000 mg	7	2.4
1250 mg	268	92.4
1500 mg	8	2.8
2000 mg	1	0.3
2500 mg	1	0.3
Unknown	3	1.0
Total	**290**	**100.0**

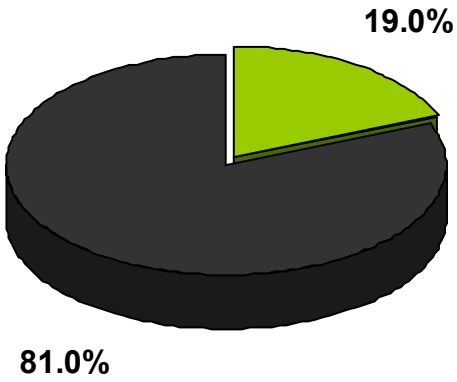
Concomitant therapy at lapatinib therapy initiation

	N	%
Capecitabin	266	91.7
Lapatinib monotherapy	16	5.5
Capecitabin+antiestrogens	2	0.7
Inhibitor aromatase	2	0.7
Vinorelbin	2	0.7
Not specified	2	0.7
Total	**290**	**100.0**

Lapatinib therapy status and reasons for therapy termination

Lapatinib therapy status

N = 290



Ongoing therapy (N = 55)

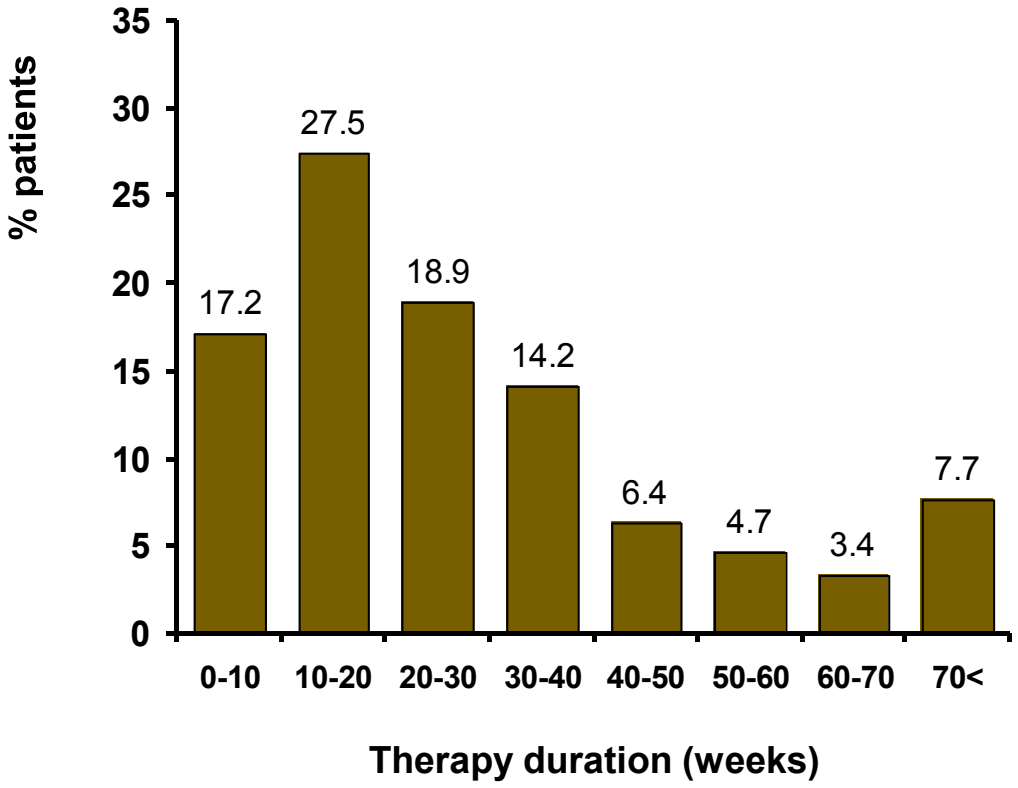
Terminated therapy (N = 235)

Reasons for therapy termination

Reason	N	%
Progression	180	76.6
Adverse effect	18	7.7
Death	11	4.7
Health status worsening without disease progression	7	3.0
Refusal	4	1.7
Other	13	5.5
Unknown	2	0.9
Total	**235**	**100.0**

Lapatinib therapy duration

N = 235 patients with terminated therapy



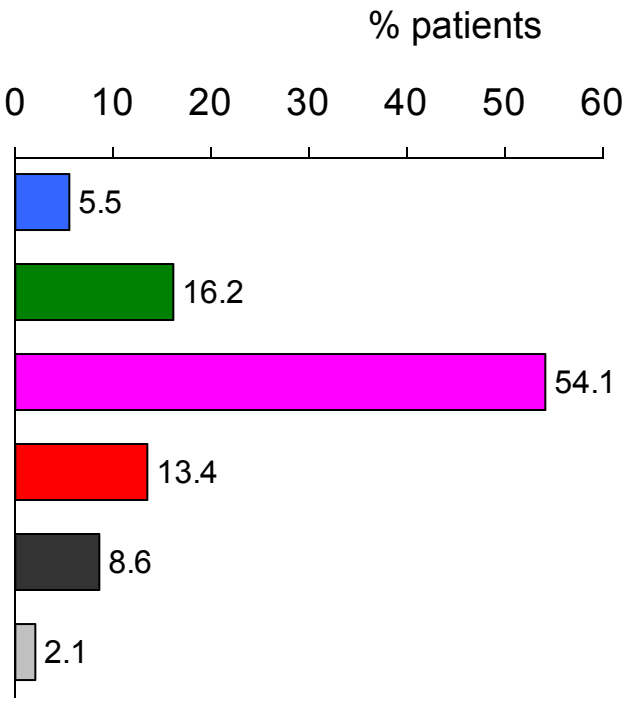
	Therapy duration
N[1)]	233
Mean	29.2 weeks
Median	21.7 weeks
5% - 95%	3.0 – 78.6 weeks

[1)] Therapy duration was not available in 2 patients.

The best response achieved in lapatinib therapy – all patients

N = 290

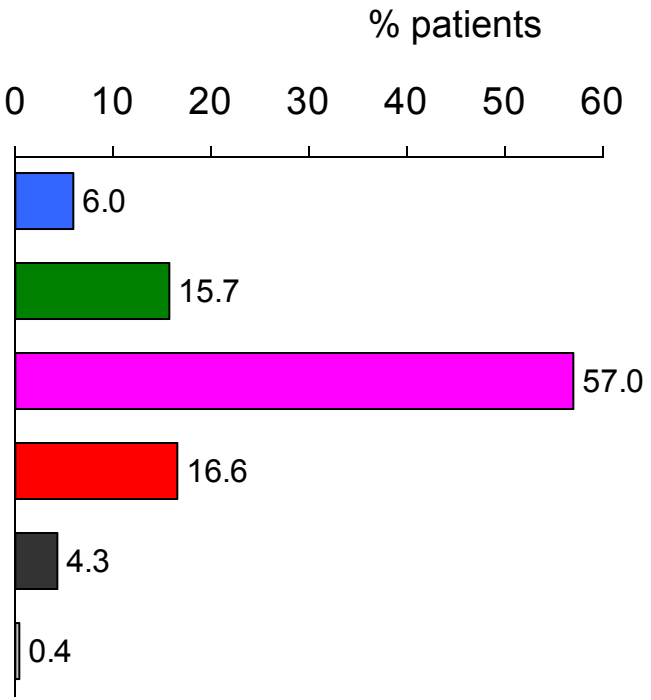
Therapy response	N	%
CR	16	5.5
PR	47	16.2
SD	157	54.1
PD	39	13.4
Not established	25	8.6
Unknown	6	2.1
Total	**290**	**100.0**



The best response achieved in lapatinib therapy - patients with terminated therapy

N = 235 patients with terminated therapy

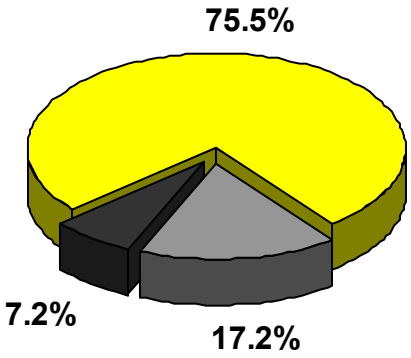
Therapy response	N	%
CR	14	6.0
PR	37	15.7
SD	134	57.0
PD	39	16.6
Not established	10	4.3
Unknown	1	0.4
Total	**235**	**100.0**



Adverse effects during lapatinib therapy

Occurrence of adverse effects

N = 290



Without (N = 219)

Adverse effects of G1 or G2 (N = 50)

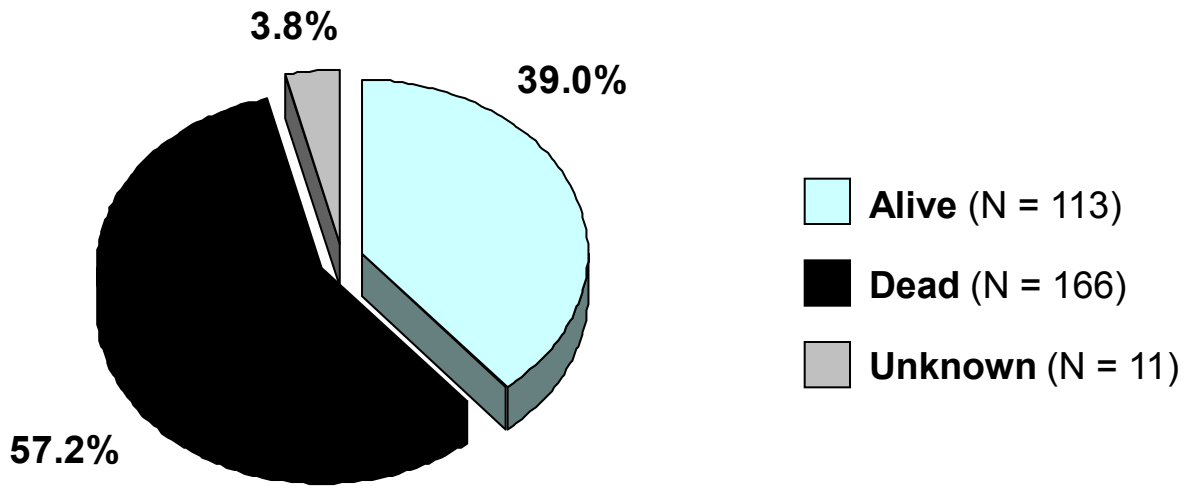
Adverse effects of G3 or G4 (N = 21)

Type of adverse effects	N (%) patients with AE G1 or G2	N (%) patients with AE G3 or G4
Diarrhoea	24 (8.3%)	12 (4.1%)
Skin toxicity	24 (8.3%)	6 (2.1%)
Nausea / vomit	11 (3.8%)	3 (1.0%)
Hepatotoxicity	8 (2.8%)	3 (1.0%)
Paronychium	2 (0.7%)	(0%)
Dyspnoe	1 (0.3%)	(0%)
Other	4 (1.3%)	2 (0.7%)

One patient can experience more adverse effects.

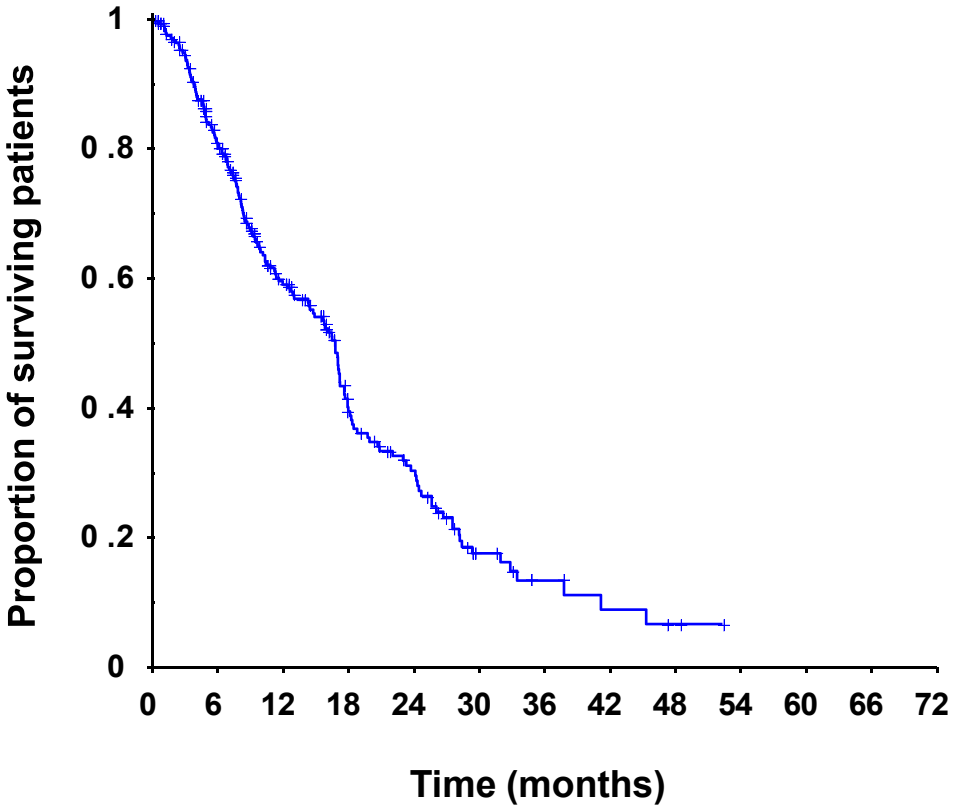
Current status of patients actually or previously treated with lapatinib

N = 290



Overall survival since lapatinib therapy initiation

N = 290

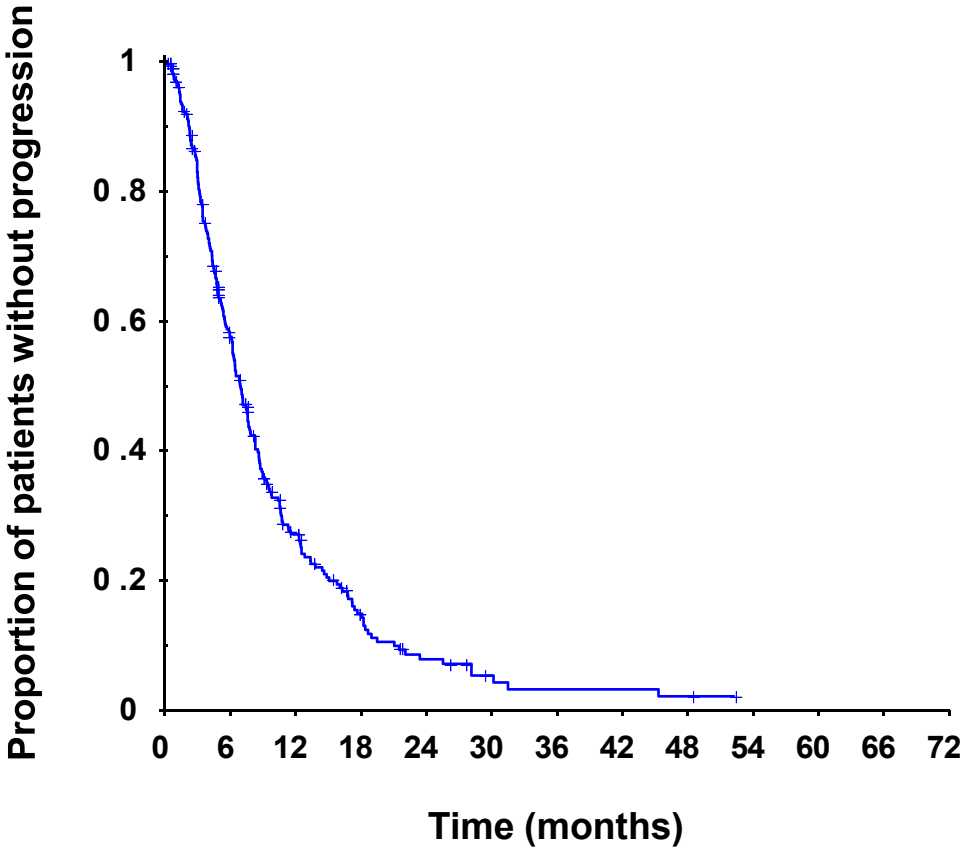


	Overall survival
Median OS (95% IS)	16.8 months (15.1; 18.5)

	Overall survival (%, 95% CI)
6-month survival	80.9 (76.1; 85.7)
1-year survival	59.1 (52.7; 65.4)
2-year survival	30.4 (23.4; 37.3)

Patients' survival was assessed by Kaplan-Meier method.

Progression-free survival since lapatinib therapy initiation



N = 290

	PFS
Median PFS (95% IS)	6,9 months (6,1; 7,7)

	PFS (%, 95% IS)
6-month survival without progression	57.6 (51.6; 63.6)
1-year survival without progression	27.2 (21.5; 32.8)
2-year survival without progression	7.9 (3.9; 11.9)

Patients' progression-free survival was assessed by Kaplan-Meier method.