Seminoma Clinical Stage 1 – Patterns of Care in Germany

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Key Words

Testicular germ cell neoplasms · Seminoma · Patterns of care · Carboplatin · Surveillance · Radiotherapy

Abstract

Introduction: International guidelines are ambivalent regarding the recommendations for the management of clinical stage 1 (CS1) seminoma. **Patients and Methods:** During 2008–2013, 1,050 patients with seminoma CS1 were prospectively registered with regard to assessing management modality (radiotherapy, carboplatin, surveillance). Associations with tumor size, rete testis invasion, age, year of diagnosis, type of institution, and geographic location were assessed. **Results:** Of the total number of patients, 49.3% received carboplatin 1 course, 8.5% carboplatin 2 courses, 35.9% surveillance, and 6.3% radiotherapy. In 2013, surveillance increased significantly to 57.9%. Treatment decisions were significantly associated with rete testis invasion and tumor size. Carboplatin was applied significantly more in office clinics than elsewhere. There is some regional variation re-

garding treatment preferences. **Conclusions:** The rising acceptance of surveillance mirrors international trends. The associations with prognostic factors demonstrate care givers to be compliant with contemporary guidelines. The association with the type of institution suggests non-oncological factors to be also relevant in decision making.

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Introduction

Testicular germ-cell tumors (GCTs) represent the most common malignancy in middle-aged men in Northern European countries [1]. Nevertheless, the mortality rates remain low, as highly effective management modalities are available [2]. Seminoma represents the most frequent histologic type comprising about 55% of GCT cases [3]. Clinical stage 1 (CS1) is defined as the absence of metastases evidenced by clinical examination, imaging studies and laboratory investigation. Today, up to 3 quarters of all seminoma cases are diagnosed with

this stage, rendering CS1 seminoma the most frequent subgroup of GCTs [4, 5], and the most important constellation of GCT in daily practice. After inguinal orchiectomy, 3 options for CS1 seminoma patients are available. Traditionally, abdominal radiotherapy was the preferred option because microscopic metastatic spread to the retroperitoneal lymph nodes and may be present despite normal imaging results [6–9]. Although radiotherapy produces excellent durable cure rates, this management strategy was challenged due to rising concerns over possible long-term toxicities as the induction of second malignancies [10]. Surveillance strategies emerged as an alternative justified by the experience of highly effective cisplatin-based therapy even in relapsing cases with advanced GCT [11, 12]. Surveillance strategies avoid any treatment toxicity until the progression of seminoma is evident. Carboplatin chemotherapy developed as a further alternative to radiotherapy because of its favorable toxicity profile [13]. Initially, this drug was administered twice with 4 weeks apart [14]. Later on, 1 course of carboplatin AUC 7 was considered effective as the original 2-course regimen [15]. All of the treatment strategies for CS1 seminoma produced long-time survival rates of at least 99% and were thus considered equivalent [16]. It is important to note that the different international guidelines on GCTs differ in their recommended management strategies for CS1 seminoma [2, 17–22]. To date, only a few studies have addressed the patterns of care regarding the management of testicular seminoma in particular countries [23]. We explored the current practice patterns regarding the treatment of CS1 seminoma in Germany. Furthermore, we evaluated possible influencing factors that might have an impact on treatment decisions.

Patients and Methods

The ‘National Seminoma Registry Study’ (NSR study) aimed at displaying the patterns of care in terms of adjuvant treatment of patients with CS1 testicular seminoma in Germany. At the outset of the study, the European consensus group recommendations authored by Krege et al. [24] represented the well-accepted standards of seminoma management. Accordingly, 4 adjuvant management modalities were considered appropriate: surveillance, abdominal radiotherapy, 1 course of carboplatin, or 2 courses of carboplatin. According to the study protocol, only the elected treatment modality was registered. Treatment decisions were correlated with the following clinical parameters: age at diagnosis (years), size of the primary tumor (cm), presence of rete testis invasion (yes/no), and the year of treatment (2008–2013). Furthermore, the following socio-epidemiological parameters were included: type of institution (university hospital, municipal hospital, office clinic) and its geographic location (according to the Zip code, ‘Postleitzahl’). For the

Table 1. Patients characteristics

	Eligible, n	
Patients, total, n	1,050	
Age, years	1,050	
Mean $\pm$ SD		41.3 $\pm$ 10.5
Median (IQR)		41 (34–48)
Range		17–82
Rete testis invasion: yes, n (%)	1,027	369 (35.9)
Tumor size, cm	1,029	
Mean		3.67 $\pm$ 2.1
Median (IQR)		3.4 (2.0–4.9)
Range		0.2–16
Year of diagnosis, n	1,050	
2008–2009		61
2010		294
2011		296
2012		202
2013		197
Type of institution, n	1,050	
University department		215
Municipal hospital		785
Office clinic		50

analysis of associations of treatment decisions with the various parameters, the 2 carboplatin regimens (1 and 2 courses, respectively) were taken as one group because the 2 procedures are not grossly different clinically, and the sample size of the 2-course group is very much smaller than that of the other group.

All patients gave informed consent to the registration for the study. The NSR study was approved by the local Ethical Committee (Ärztchamber Hamburg, PV 3123).

From 2008 to 2013, a total of 1,050 patients with testicular seminoma CS1 were prospectively registered from 130 urologic institutions in Germany. A list of the participating institutions, ranked according to the number of cases enrolled is given in the appendix. Clinical details and socioepidemiological features of the entire cohort are given in table 1.

All of the data were prospectively filed in a commercially available database system (MS Excel). We evaluated the relative frequency of the management modalities for the entire study period (2008–2013). 95% CIs were calculated for proportions. We then calculated the relative frequency of each applied management modality per consecutive years of the study period. The chi-square test was used to test for temporal trends across years and for associations of treatment decisions with rete testis invasion and the type of institution. Associations of the management decisions with tumor size and patient age were evaluated with the Kruskal–Wallis test. Possible associations with the location of the institution were analyzed by descriptive methods. Because of underprovided data from several German federal states (Bundesländer), the statistical analysis involved only pairwise comparisons with the chi-square test using the federal state of Hamburg as reference. All of the final statistical analyses were performed with the SAS software package version 9.3 (SAS Institute, Inc., Cary, N.C., USA) on a Windows platform.

Table 2. Utilization of treatment modalities during the entire observation period 2008–2013

	n	%	95% CI ^a
<i>Treatment modality</i>			
Surveillance	377	35.9	32.2–39.7
Radiotherapy	66	6.3	4.6–8.3
Carboplatin 1 course	518	49.3	45.4–53.2
Carboplatin 2 courses	89	8.5	6.5–10.8
<i>Treatment modality (carboplatin 1 group)</i>			
Surveillance	377	35.9	32.2–39.5
Radiotherapy	66	6.3	4.7–8.3
Carboplatin	607	57.8	54.1–61.5
Total	1,050	100	

^a Multinomial exact CI.

Fig. 1. Utilisation of treatment modalities – changes over time.

Table 3. Treatment modalities grouped by year of treatment

Year of diagnosis, n (%)	Surveillance (n = 377)	Radiotherapy (n = 66)	Carboplatin 1 course (n = 518)	Carboplatin 2 courses (n = 89)	Total (n = 1,050)	Pairwise p values (chi-square test) ^a
2008–2009	16 (26.2)	4 (6.6)	34 (55.7)	7 (11.5)	61 (100.0)	<0.0001
2010	59 (20.1)	31 (10.5)	173 (58.8)	31 (10.5)	294 (100.0)	<0.0001
2011	101 (34.1)	18 (6.1)	149 (50.3)	28 (9.5)	296 (100.0)	<0.0001
2012	87 (43.1)	9 (4.5)	90 (44.6)	16 (7.9)	202 (100.0)	0.009
2013	114 (57.9)	4 (2.0)	72 (36.5)	7 (3.6)	197 (100.0)	
Over-all p value (chi-square test)						<0.0001

^a The year 2013 is reference for pairwise comparisons.

Results

The most frequent treatment modality was one course of carboplatin, which was applied in 49.3% of the cases. Noteworthy, radiotherapy was applied only to 6.3% of the seminoma patients. The relative frequencies of the treatment modalities are given in table 2.

There was a significant shift over time regarding the relative frequencies of treatment modalities from 2008 to 2013 ($p < 0.0001$). Surveillance ranked second in 2008 behind carboplatin and experienced a constant increase ever since to become the first ranking modality with 57.9% of the cases in 2013. Details are given in table 3 and figure 1.

The tumor size was significantly associated with the treatment decisions (table 4). Patients allocated to sur-

veillance had a significantly smaller median tumor size (2.6 cm) than those submitted to radiotherapy (4.1 cm) and carboplatin (4.0 cm) ($p < 0.0001$). Upon categorizing tumor size by 1 cm increments, surveillance is the most frequent modality among patients with tumor size of less than 2 cm (51.0% of this category, 10.7% of all cases). Among those with tumors larger than 5 cm, carboplatin is the predominant treatment modality (76.0% of this category, and 18.9% of all cases; $p < 0.0001$).

Rete testis invasion is likewise associated with the treatment decisions (table 4). Only 19.8% of patients with rete testis invasion were submitted to surveillance, while the remainder received carboplatin or adjuvant radiotherapy, respectively (72.9 and 7.3%; $p < 0.0001$).

Age was not associated with the treatment decisions (table 4) by overall analysis. Yet, by pairwise comparison

Table 4. Association of treatment decisions with clinical factors (the 2 carboplatin groups are grouped)

	Surveillance (n = 377)	Radiotherapy (n = 66)	Carboplatin (n = 607)	Total (n = 1,050)
Tumor size, cm				
Eligible, n	372	65	592	1,029
Mean (SD)	2.96 (1.69)	4.05 (2.13)	4.07 (2.21)	3.67 (2.10)
Median (IQR)	2.60 (1.80–4.00)	4.10 (2.50–5.00)	4.00 (2.40–5.30)	3.40 (2.00–4.90)
Range	0.5–11.0	0.6–14.0	0.2–16.0	0.2–16.0
Missing information	5	1	15	21
p value (Kruskal–Wallis test)				<0.0001
Pairwise p values (Kruskal–Wallis test) ^a		<0.0001	<0.0001	
Rete testis invasion, n (%)				
No	295 (44.8)	37 (5.6)	326 (49.5)	658 (100.0)
Yes	73 (19.8)	27 (7.3)	269 (72.9)	369 (100.0)
Missing information	9 (39.1)	2 (8.7)	12 (52.2)	23 (100.0)
p value (chi-square test)				<0.0001
Pairwise p values (chi-square test) ^a		<0.0001	<0.0001	
Age at diagnosis, years				
Mean (SD)	40.5 (10.7)	41.7 (9.3)	41.7 (10.5)	41.3 (10.5)
Median (IQR)	40.0 (33.0–47.0)	41.0 (35.0–45.0)	42.0 (34.0–48.0)	41.0 (34.0–48.0)
Range	20–82	25–73	17–82	17–82
p value (Kruskal–Wallis test)				0.1367
Pairwise p value (Kruskal–Wallis test) ^a		0.4450	0.0484	

^a Reference for pairwise comparisons: surveillance. IQR = Interquartile range.

with surveillance, carboplatin treatment was associated with older age ($p = 0.0484$).

The type of institution had a significant influence on the treatment decision (table 5; $p = 0.0093$). University hospitals did more frequently advocate surveillance strategies (45.1% of their patients) than municipal hospitals (33.8%) and office clinics (30%). Conversely, carboplatin was the most frequent modality chosen in office clinics (68.0% of their patients), while municipal hospitals (59.1%) and university departments (50.7%) applied this therapy less frequently ($p = 0.0104$).

The evaluation of possible associations of treatment decisions with geographic regions is hampered by a skewed distribution of the study population across the German federal states. Roughly two thirds of the entire study population ($n = 765$) derive from the 5 federal states Baden–Württemberg, Hamburg, Bayern, Niedersachsen and Nordrhein–Westfalen, while the other eleven countries contribute only one third of the population. If exclusively the former 5 regions were evaluated (table 6), there was indeed some variance visible regarding the preferences for a particular treatment modality. Bayern ranked first in applying radiotherapy to 20.9% of the patients

($p < 0.0001$). Niedersachsen ranked first with the application of carboplatin chemotherapy to 70.7% of the patients ($p = 0.0478$). Baden–Württemberg ranked first with respect to surveillance with 48.6% of the patients ($p = 0.3575$, not significant).

Discussion

This is the first evaluation of patterns of care of CS1 seminoma in Germany. The most striking result is the continuous rise of surveillance during the study period until it became the preferred treatment modality in 2013. At the same time, we noted a shift from carboplatin chemotherapy that ranked first in 2008 to surveillance ranking first in 2013. Probably, the European Association of Urology guidelines that were newly re-issued in 2011 [2] had a significant bearing on treatment decisions, particularly, as these guidelines are popularized by the well-accepted second opinion network for GCT in Germany [25, 26]. The rising trend of surveillance in Germany was first observed in an evaluation of the second opinion network in 2013 [27]. A survey

Table 5. Association of treatment decision with type of institution

Type of institution, n (%)	Surveillance (n = 377)	Radiotherapy (n = 66)	Carboplatin (n = 607)	Total (n = 1,050)	Pairwise p values (chi-square test) ^a
Office clinic	15 (30.0)	1 (2.0)	34 (68.0)	50 (100.0)	0.0839
Municipal hospital	265 (33.8)	56 (7.1)	464 (59.1)	785 (100.0)	0.0056
University department	97 (45.1)	9 (4.2)	109 (50.7)	215 (100.0)	
Overall p value (chi-square test)				0.0093	
^a Reference for pairwise comparisons: University department.					

Table 6. Treatment decisions in select German federal states

Country, n (%)	Surveillance (n = 377)	Radiotherapy (n = 66)	Carboplatin (n = 607)	Total (n = 1,050)	Pairwise p value (chi-square test) ^a
Baden-Württemberg	67 (48.6)	5 (3.6)	66 (47.8)	138 (100)	0.3575
Bayern	29 (26.4)	23 (20.9)	58 (52.7)	110 (100)	<0.0001
Hamburg	99 (44.4)	4 (1.8)	120 (53.8)	223 (100)	
Niedersachsen	21 (18.0)	1 (1.3)	53 (70.7)	75 (100)	0.0376
Nordrhein-Westfalen	75 (34.2)	9 (4.1)	135 (61.6)	219 (100)	0.0478
All other states	86 (30.2)	24 (8.4)	175 (61.4)	285 (100)	<0.0001
^a Reference for pairwise comparison is Hamburg.					

among physicians treating seminoma patients in Europe revealed greatly differing treatment recommendations among various specialties and countries [28]. In the United Kingdom (UK), a decrease of radiotherapy utilization has been observed to a similar extent as documented in Germany and also Scandinavia [29]. Currently, up to 66% of seminoma patients receive carboplatin chemotherapy in the United Kingdom; however, simultaneously, surveillance is gaining acceptance [30]. A recent report from Australia revealed that carboplatin was the most accepted treatment modality comprising about 62% of patients. About 33% are referred to surveillance regimens and only 5% receive radiotherapy [31]. Noteworthy, radiotherapy is still the most popular treatment for seminoma patients in the United States and in Eastern European countries [28, 32]. However, surveillance and carboplatin are slowly gaining shares [33].

The evaluation of practice patterns is a rather new field of clinical research [34]. Formal clinical trials usually enroll highly selected patients and apply high and rigid standards of quality control. However, daily clinical practice is different and often, the excellent results of

pace-making clinical trials are not fully reproducible in clinical reality [35]. Patterns of care analyses aim to unveil this gap between scientific trials and clinical reality and seek to open avenues to narrow the gap [36]. With regard to testicular cancer, a number of patterns of care analyses have already been reported on the international level [4, 37, 38]. In Germany, the current study is the first one to analyze on a national level how guideline recommendations accord with the way testicular cancer patients are actually treated.

Another notable result of this study is the association of treatment decisions with various parameters. Expectedly, the established prognostic parameters for tumor progression, that is, tumor size and rete testis invasion [39] were significantly associated with treatment decisions. This observation is in accordance with the current guidelines and suggests that guidelines are accepted in daily practice.

Higher age is weakly associated with the decision for carboplatin chemotherapy. This result is surprising as younger age has been suggested to be a prognostic factor for progression [40]. Accordingly, one could have expected more decisions for carboplatin in younger patients. On

the other hand, sound evidence on the association of younger age and progression is still lacking, partly explaining our unexpected observation.

Treatment decisions might well have been influenced by other factors, for example, the patient's mental status, the wish for paternity, job-related problems, and other sociodemographic factors. Also, the presence of contralateral testicular intraepithelial neoplasia could impact on decision making. However, all of these aspects could not be explored with the tools used in this study.

Another surprising result is the association of treatment decisions with the type of institution. The reasons why office clinics prefer carboplatin regimens remain elusive. Possibly, reasons beyond clinico-oncological considerations as economic incentives might affect decision making in the office clinic setting, but evidence for this hypothesis is lacking. University departments are dedicated to acknowledge new ideas and to test novel treatment strategies. Thus, surveillance, which represents the most novel strategy in seminoma might be predominantly applied by university departments.

The differences of practice patterns between different German federal states as observed in this study should be interpreted carefully because of underprovided data from several federal states. Statistical bias cannot be ruled out since numbers are small in the particular subgroups. On the other hand, 4 of the larger states (Nordrhein-Westfalen, Baden-Württemberg, Bayern, and Niedersachsen) were well represented in the study, allowing at least some cautious explorations. A striking finding is the persisting high utilization of radiotherapy with 20% of cases in Bayern. This finding disaccords with national and international trends [29, 41, 42] and is at variance with the recent guideline recommendations [2] and the nationwide operating second opinion network on GCT [25]. The preference of surveillance regimens observed in Baden-Württemberg may be related to the high number of patients recruited from university departments in this state, as surveillance according to our findings was the preferred treatment modality in university departments.

Strengths of this study involve the prospective way of patient recruitment as well as the large number of CS1 patients included. The number of missing parameters per case is low; thus, the data can be considered robust. As we only noted the treatment recommendation given by the institution performing the primary management (i.e. orchiectomy and primary staging), we do not know whether or not these recommendations had been followed in the later course. The lack of information re-

garding the compliance of local physicians with the original recommendations is a clear limitation of the study. However, confounding the study results by noncompliance is probably low because in most of the cases the adjuvant treatment recommended is usually applied in the same institution. Only surveillance strategies are implemented by office urologists. Another limitation is clearly the voluntary study character because in this setting (other than in a compulsory registry), several centers apparently did not report all of the seminoma cases treated. This view is substantiated by the low number of registered patients in many of the participating centers although higher incidence rates were likely prevalent. However, in light of a lacking National Cancer registry in Germany with compulsory documentation of clinical data by treatment providers, a more accurate description of the patterns of care seems hardly possible in this country.

Conclusion

This study is the first patterns-of-care analysis regarding the management of CS1 testicular seminoma patients in Germany. A significant increase in surveillance regimens was documented with a simultaneous decrease of carboplatin chemotherapy. Treatment decisions were associated with the known prognostic factors of tumor size and rete testis invasion. Age was only weakly associated with treatment decision. One unexpected result was the association of treatment decisions with the type of institution. In particular, the preference of carboplatin therapy in office clinics and the preference of surveillance in university departments have been documented for the first time. In terms of regional variances, an ongoing high utilization of radiotherapy in Bayern and a high rate of surveillance in Baden-Württemberg was notable.

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Disclosure Statement

The authors declare no conflicts of interests with the article.

Appendix

Contributing Institutions Ranked by the Number of Cases Enrolled

Hamburg, Bundeswehr Krankenhaus	Berlin, Universitätsklinikum Charité
Hamburg, Albertinen-Krankenhaus	Bonn, Waldkrankenhaus
Tuebingen, Urologische Universitätsklinik	Erfurt, Krankenhaus St. Nepomuk
Trier, Krankenhaus der Barmherzigen Brüder	Hameln, Kreiskrankenhaus
Mannheim, Urologische Universitätsklinik	Koblenz, Bundeswehrkrankenhaus
Lohne, St. Franziskus Krankenhaus	Lübeck, Universitätsklinikum Schleswig-Holstein
Bonn, Urologische Universitätsklinik	Reifenstein, Eichsfeld Klinikum
Siegen, Jung-Stilling Krankenhaus	Wetzlar, Klinikum
Ahaus, St. Marien Krankenhaus	Datteln, St. Vincenz Krankenhaus
Chemnitz, Zeisigwaldklinik	Fürth, Klinikum
Leipzig, St. Elisabeth Krankenhaus	Garmisch-Partenkirchen, Klinikum
Berlin, St. Hedwig Krankenhaus	Gießen, Urologische Universitätsklinik
Freiburg, Universitätsklinik	Kempten, Klinikum
Karlsruhe, Städtisches Klinikum	Köln, Urologische Universitätsklinik
Gladbeck, St. Barbara Hospital	Mannheim, Diakonie-Krankenhaus
Bergisch Gladbach, Marien-Krankenhaus	Pforzheim, Siloah St. Trudpert Klinikum
Köln, Heilig Geist Krankenhaus	Schwerin, Helios Kliniken
Köln, Urologgia	Stralsund, Helios Hanse Klinikum
Magdeburg, Universitätsklinik	Wilhelmshaven, Reinhard-Nieter-Krankenhaus
Münster, Universitätsklinik	Bad Bergzabern, Klinikum Landau
Reichenbach, Paracelsus-Klinik	Baden-Baden, Dr. Brüggeboes
Amberg, Klinikum St. Marien	Bautzen, Oberlausitzkliniken
Berlin, Bundeswehrkrankenhaus	Berlin, Helios Kliniken
Coburg, Städtisches Klinikum	Berlin, Vivantes Auguste-Victoria-Krankenhaus
Kaiserslautern, Westpfalzkl. Klinikum	Dresden, Diakonissenkrankenhaus
Gütersloh, Städtisches Klinikum	Fürstenfeldbruck, Urologisches Zentrum
München, Klinikum Bogenhausen	Hamm, St. Josef Krankenhaus
Ulm, Bundeswehrkrankenhaus	Homburg, Urologische Universitätsklinik
Würzburg, Julius Maximilian Universität	Münster, Herz-Jesu-Krankenhaus
Frankfurt, Universitätsklinik	Nürnberg, ÜGP
Fulda, Klinikum	Solingen, Städtisches Klinikum
Rüsselsheim, Klinikum	Ulm, Urologische Universitätsklinik
Schweinfurt, Leopoldina-Krankenhaus	Augsburg, Klinikum
Erlangen, Waldkrankenhaus St. Marien	Bad Hersfeld, Klinikum
Flensburg, Diako Klinikum	Bamberg, Klinikum Bruderwald
Frankfurt, Städtische Kliniken Höchst	Bonn, Malteser Krankenhaus
Klinikum Ingolstadt	Detmold, Klinikum Lippe
Köln, St. Elisabeth Krankenhaus	Frankfurt, Praxisklinik Prof. Bickeböller
Lübecke, Krankenhaus	Gehrden, Robert-Koch-Krankenhaus
Bad Tölz, Asklepios Stadtklinik	Göttingen, Evangelisches Krankenhaus Weende
Hamm, St. Barbara Klinik	Hamburg, Praxisklinik Dr. Heitz
Herzberg, Urologie Herzberg	Hamburg, Praxisklinik Dr. Soyka
Jena, Urologische Universitätsklinik	Hamburg, Universitätsklinikum Eppendorf
Löningen, St. Anna Stift	Hannover, Friederikenstift
Mönchengladbach, Maria Hilf Krankenhaus	Heidelberg, Krankenhaus Salem
Schwäbisch Hall, Diakonie Klinikum	Itzehoe, Klinikum
Aachen, Urologische Universitätsklinik	Lauchhammer, Klinikum Niederlausitz
Freiberg, Kreiskrankenhaus	Lüdenscheid, Märkische Kliniken
Gera, Waldklinikum	Magdeburg, Klinikum
Göttingen, Urologische Universitätsklinik	Nürnberg, Theresien-KH
Köln, Dr. Klier	Rostock, Urologische Universitätsklinik
Geestland, Seepark Klinik	Schwedt, Asklepios Klinik
Plauen, Helios Klinikum	Stuttgart, Katharinenhospital
Aschersleben, Kreiskliniken	Würzburg, Julius-Spital

Amberg, Praxisklinik Dres. Scharl/Vogel/Schreyer
 Bad Nauheim, Praxisklinik Dr. Focke
 Bitburg, Praxisklinik Dres. Zender/Müller
 Bremen Praxisklinik am Klinikum Bremen-Nord
 Bremen, Klinikum Bremen-Mitte
 Deggendorf, Klinikum
 Dessau, Diakonie-Krankenhaus
 Frechen, St. Katharinen Krankenhaus
 Hamburg, Asklepios Klinik Barmbek
 Hamburg, Praxisklinik Dr. Bünz
 Hannover, Siloah Krankenhaus

Herne, Marienhospital
 Kempen, Hospital zum Heiligen Geist
 Köln, Krankenhaus Holweide
 Marktredwitz, Klinikum Fichtelgebirge
 Memmingen, Klinikum
 München, Urologische Universitätsklinik Großhadern
 Pfullingen, Praxisklinik Dr. Pesendorfer
 Schwedt, Klinikum Uckermark
 Weiden, Klinikum
 Wesel, Marien-Hospital
 Zirndorf, Praxisklinik Dr. Bismarck

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