

Second malignancies in CML treated with tyrosine kinase inhibitors in the Czech Republic and Slovakia

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on behalf of CAMELIA and INFINITY registries

Information on the second malignances in CML during imatinib treatment

Poitiers, Cedex, France: 189 CML patients treated with imatinib

Observed ratio of the **second cancers** and **prostate** cancer: **547.4 per 100 000 person-years (PY)** and **478.5 per 100.000 PY**.

Roy L, et al. Leukemia 2005; 19: 1689-1692.

Data on file Novartis

The observed incidence was **720.34 per 100 000 PY** for all **second cancers** (excluding nonmelanoma skin cancer) and **262.01 per 100 000 PY** for **prostate cancer**.

Pilot PR, et al. Leukemia 2006; 20: 148. (online 14 July 2005.)

<http://cmlsupport.blogspot.com/2006/03/epidemiological-analysis-of-second.html>

ILTE study: 957 (948) patients

Second cancers in 28 patients (rate **1.1/100 PY**); observed/expected ratio 1.27 (95% CI = 0.84-1.84).

Second cancers in 29 patients (rate **0.9/100 PY**), with an observed/expected ratio of 1.02.

Gambacorti-Passerini C, et al. 50th ASH San Francisco, December 6, 2008; Blood 2008; 112: 401, #1099.

Kim DW, et al. 51st ASH New Orleans, December 6, 2009; Blood 2009; 114: #2199.

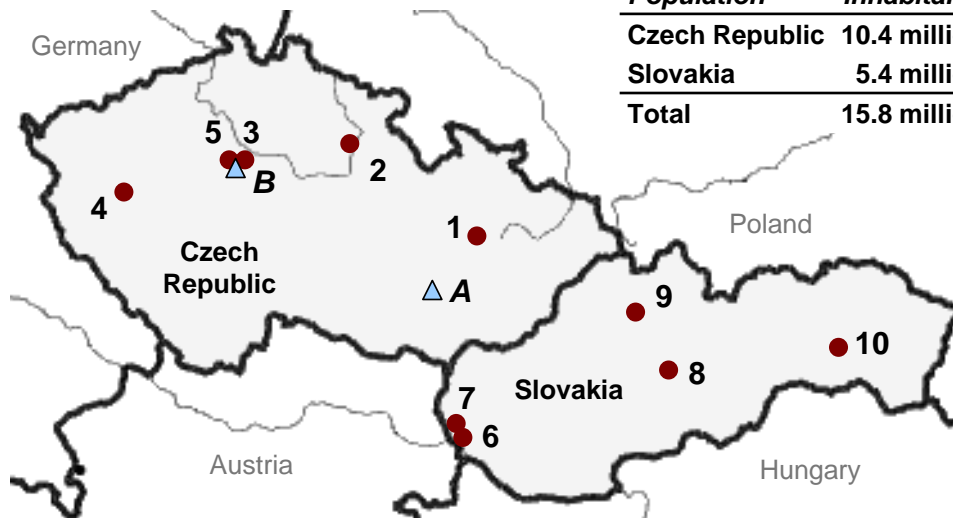
M.D. Anderson Cancer Center: 1647 pts treated with TKIs

A total of 67 (**4.07%**) patients (47 male, 20 female) **developed a second cancer**; 46 (**2.8%**) patients second cancer **with exclusion of non-melanoma skin cancer**.

Verma D, et al. 50th ASH San Francisco, December 7, 2008; Blood 2008; 112: 740, #2125.

Data available in the Czech Republic and Slovakia

CML centres in the Czech Republic and Slovakia participating in this study:



<i>Population</i>	<i>Inhabitants</i>
Czech Republic	10.4 million
Slovakia	5.4 million
Total	15.8 million

● CAMELIA study group:



Czech Republic

1. University Hospital Olomouc
2. University Hospital Hradec Králové
3. University Hospital Královské Vinohrady Praha
4. University Hospital Plzeň
5. General University Hospital Praha

Slovakia

6. University Hospital and Health Centre Bratislava
7. National Cancer Institute Bratislava
8. FD Roosevelt University Hospital Banská Bystrica
9. University Hospital Martin
10. L. Pasteur University Hospital Košice

△ INFINITY study group:



Czech Republic

- A. University Hospital Brno
- B. The Institute of Hematology and Blood Transfusion Praha

Ph+ CML patients treated with imatinib during years 2000 – 2007:

CAMELIA study group	524 patients
INFINITY study group	265 patients
Total	789 patients

Ph+ CML patients treated with imatinib in years 2000-2007

N = 789

Gender

Men	407 (52 %)
Women	382 (48 %)

Imatinib treatment

1st line	397 (50 %)
2nd line	392 (50 %)

Age

Mean	49 years
Median	51 years
Range	15 – 81 years

Follow-up after CML diagnosis

Mean	54 months
Median	43 months
Range	1 – 228 months

Follow-up after initiation of imatinib

Mean	35 months
Median	34 months
Range	1 – 91 months

Ph+ CML patients treated with imatinib with second malignancies in years 2000-2007

Patient	Sex	Age at CML [years]	CML treatment (drugs)	Site of SM	Age at SM [years]	OS _{CML} [months]	Status (cause of death)
1	F	72	HY,IM	Pancreas	74	12	SM
2	M	54	HY,INF,IM	Colon	61	110	alive
3	M	36	BU,HY,INF,IM	Testis	52	192	SM
4	F	56	HY,INF,IM	Skin	58	80	alive
5	M	49	CH,IM,D	Kidney	54	58	CML
6	M	40	HY,INF,AraC,IM	Caecum	52	144	SM
7	F	48	HY,INF,IM	Breast	50	33	alive
8	M	71	HY,INF,IM	Hematopoietic tissue	76	97	alive
9	M	74	HY,INF,AraC,IM	Vater's papilla	80	70	SM
10	F	32	HY,IM,SCT	Cervix uteri	33	57	alive
11	M	51	HY,INF,IM	Prostate	59	100	alive
12	M	67	IM	Bronchus and lung	70	29	SM
13	M	45	HY,INF,IM	Lung	50	56	alive
14	F	50	INF,IM	Breast	56	71	other
15	F	64	IM	Breast	65	13	SM
16	M	69	IM	Lung	71	28	alive
17	F	52	HY,INF,AraC,IM,D	Skin	63	142	CML
18	M	53	HY,INF,IM	Small intestine	55	51	alive
19	M	71	HY,IM	Larynx	72	13	alive
20	M	68	HY,IM, D	Prostate	70	28	alive
21	F	71	HY,IM	Uterus	76	64	other
22	M	58	HY,INF,IM	Skin	65	84	SM
23	M	42	INF,AraC,IM	Colon	48	96	alive
24	F	40	INF,AraC,IM	Pancreas	48	91	alive
25	F	61	autoSCT,IM	Myeloma	61	27	alive
26	F	49	INF,IM	Breast	53	139	alive
27	M	46	HY,INF,IM	Lymphoma of stomach	52	85	alive
28	M	60	HY,INF,IM	Kidney, prostate, glioblastoma	61	70	SM

Abbreviations: CH = chemotherapy, BU = busulphan, HY = hydroxyurea, INF = interferon, AraC = cytosinarabinosid, SCT = stem cells transplantation, IM = imatinib, D = dasatinib, SM = second malignancy, CML = chronic myeloid leukemia

Ph+ CML patients treated with imatinib with second malignancies in years 2000-2007

Second malignancy developed in 28 (3.55 %) of 789 CML patients.

Gender

Men	17 (61 %)
Women	11 (39 %)

Age at diagnosis

Mean	55 years
Median	53 years
Range	32 – 74 years

Age at second malignancy

Mean	60 years
Median	59 years
Range	33 – 80 years

In 25 (3.17 %) of 789 CML patients second malignancy (SM) developed **after imatinib therapy**.

Imatinib treatment

1 st line	7 (28 %)
2 nd line	18 (72 %)

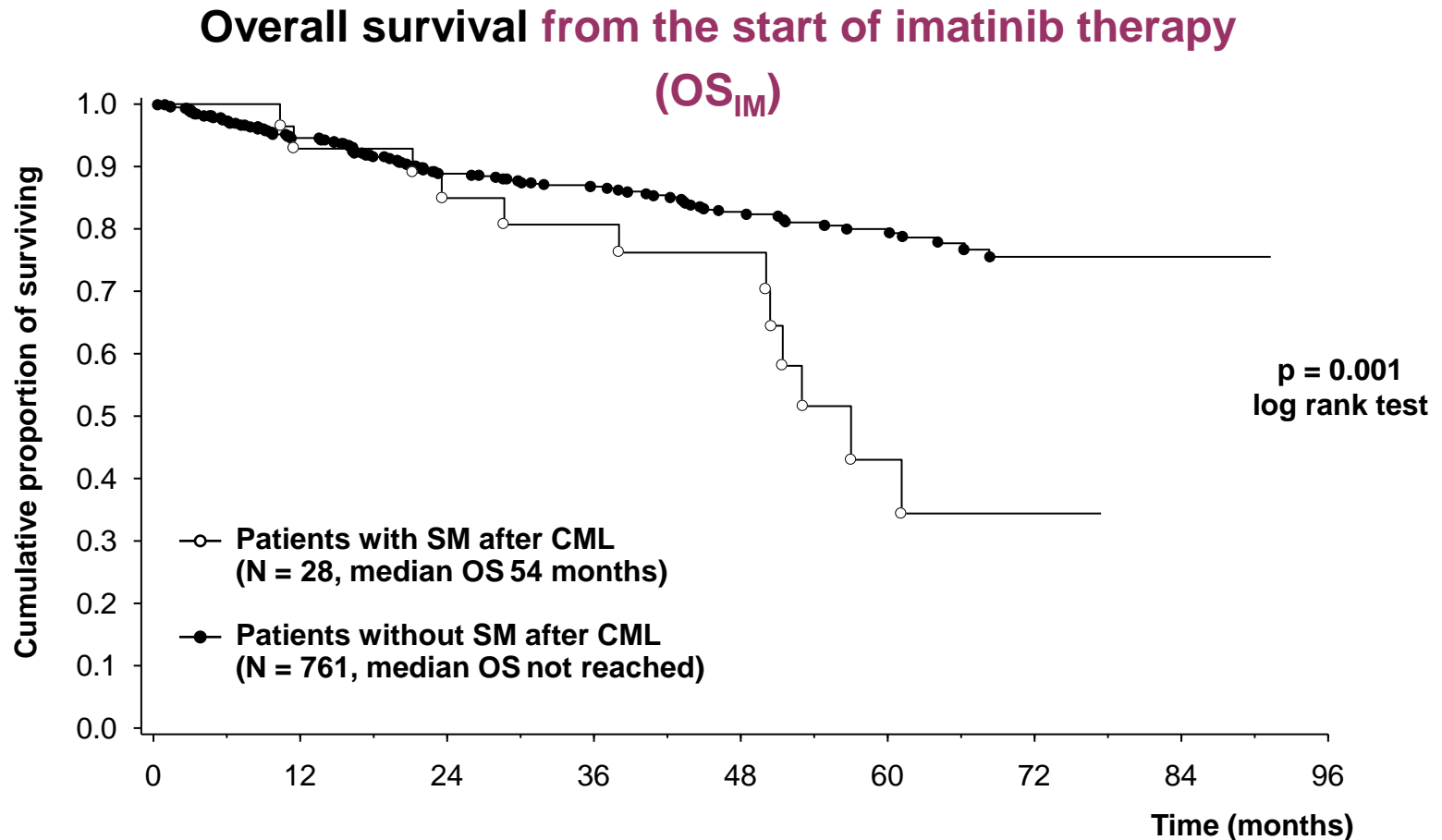
Time from CML diagnosis to SM

Mean	58 months
Median	56 months
Range	7 – 184 months

Time from the start of IM therapy to SM

Mean	29 months
Median	29 months
Range	2 – 57 months

Overall survival of Ph+ CML patients with and without second malignancies (SM)



Status of 28 patients with SM after CML:

Alive	16 (57 %)
Died	12 (43 %)
- SM	8 (29 %)
- CML	2 (7 %)
- other	2 (7 %)

Incidence of second malignancies in CML patients treated with imatinib

In 25 (3.17 %) of 789 CML patients second malignancy developed **after imatinib therapy**.

Follow-up from the start of imatinib was 2641 person-years in 789 CML patients.

Observed incidence of all second malignancies on imatinib treatment was 946.6 per 100,000 person-years.

Comparison of cancer incidence in whole population and in CML patients treated with imatinib

Incidence of all cancers in whole population of the Czech Republic and Slovakia aged 15–85 years was 647.2 per 100,000 person-years in years 2000–2004.

Source:

Czech National Cancer Registry: Cancer incidence in the Czech Republic, Institute of Health Information and Statistics of the Czech Republic, Prague 2008; 254 p. ISBN 978-80-7280-723-9

Slovak National Cancer Registry: Cancer Incidence in Slovak Republic, National Health Information Center of Slovak Republic, Bratislava 2008, 16 9p. ISBN 978-80-89292-04-2

Incidence of all cancers in patients treated with imatinib aged 15–85 years was 1156.9 per 100,000 person-years when age-standardized to the entire population.

Observed incidence of the second malignancies in CML patients treated with imatinib was 1.79 times higher than the incidence in the general population.

Conclusions

- **Second malignancies in patients with CML represent serious complication that affects quality of life and survival of patients depending on its curability.**
- **Interpretation of our observation must be very cautious. Incidence of second malignancies in our study are in line with relative cancer incidence in the Czech Republic.**
- **Longer follow-up of a larger numbers of patients treated with TKI is needed to clarify the true incidence of second malignancies in patients with CML: **the role of ELN registry.****

Acknowledgements



Voglová J, Hradec Králové, CZ
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