ESR1 mutations and use of the oral SERD elacestrant in metastatic breast cancer patients in Austria: Results from the AGMT_MBC-Registry

Simon Peter Gampenrieder[1,2,3], Gabriel Rinnerthaler[2,3,4], Angelika Pichler[5], Walter Herz[6], Renate Pusch[7], Clemens Dormann[7], Christoph Suppan[4], Margit Sandholzer[8], Thomas Winder[8], Sonja Heibl[3,9], Lukas Scagnetti[9], Clemens Schmitt[10], August Felix Zabernigg[11], Daniel Egle[12], Christopher Hager[13], Petra Pichler[14], Florian Roitner[15], Johannes Andel[16], Kathrin Strasser-Weippl[17], Rupert Bartsch[18], Vanessa Castagnaviz[1], Michael Hubalek[19], Michael Knauer[20], Christian Fridolin Singer[21], Richard Greil[2,3,22,23]

[1] Department of Internal Medicine III with Haematology, Medical Oncology, Haemostaseology, Infectiology and Rheumatology, Oncologic Center, Paracelsus Medical University Salzburg, Salzburg, Austria; [2] Cancer Cluster Salzburg, Salzburg, Austria; [3] Austrian Group for Medical Tumor Therapy (AGMT) GmbH, Salzburg, Austria; [4] Internal Medicine - Department for Haemato-Oncology, LKH Hochsteiermark, Leoben, Austria; [5] Department of Surgery, Breast Health Center, LKH Hochsteiermark, Leoben, Austria; [6] Internal Medicine I for Hematology with Stem Cell Transplantation, Hemostaseology and Medical Oncology, Ordensklinikum Linz Barmherzige Schwestern – Elisabethinen, Linz, Austria; [7] Division of Oncology, Department for Internal Medicine, Medical University Graz, Graz, Austria; [8] Department of Internal Medicine II, Academic Teaching Hospital Feldkirch, Feldkirch, Austria; [9] Department of Internal Medicine IV, Klinikum Wels-Grieskirchen GmbH, Wels, Austria; [10] Department for haematology and internal oncology, Med Campus III, Kepler University Hospital Linz; [11] Department of Internal Medicine, County Hospital Kufstein, Kufstein, Austria; [12] Department of Gynaecology, Medical University Innsbruck, Innsbruck, Austria; [13] Breast Center Dornbirn, Dornbirn, Austria; [14] Department for Internal Medicine 1, University Hospital St.Pölten, St. Pölten, Austria; [15] Department of Internal Medicine II, Hospital Braunau, Braunau, Austria; [16] Department of Internal Medicine II, Pyhrn-Eisenwurzen Klinikum Steyr, Steyr, Austria; [17] Department of Medicine I, Clinic Ottakring, Vienna, Austria; [18] Department of Medicine I, Division of Oncology, Medical University of Vienna, Vienna, Austria; [19] Department of Gynecology, Breast Health Center Schwaz, Schwaz, Austria; [20] Tumor and Breast Center Eastern Switzerland, St. Gallen, Switzerland; [21] Department of Obstetrics and Gynecology and Comprehensive Cancer Center, Medical University of Vienna, Vienna, Austria; [22] Salzburg Cancer Research Institute-Laboratory for Immunological and Molecular Cancer Research (SCRI-LIMCR), Salzburg, Austria; [23]Salzburg Cancer Research Institute-Center for Clinical Cancer and Immunology Trials (SCRI-CCCIT) GmbH, Salzburg, Austria

Background

Elacestrant is the first oral Selective Estrogen Receptor Degrader (SERD) to be approved in the EU as of September 2023. Since its approval, testing for mutations in the estrogen receptor 1 (ESR1) gene has become standard care for patients with hormone receptor (HR)-positive, HER2-negative metastatic breast cancer (MBC) in low- to intermediate risk disease. ESR1 mutations are a known mechanism of resistance to aromatase inhibitors (AIs), with their frequency significantly increasing after AI treatment. This study presents the first real-world data from the Austrian Study Group of Medical Tumor Therapy (AGMT) MBC Registry regarding ESR1 testing and elacestrant use.

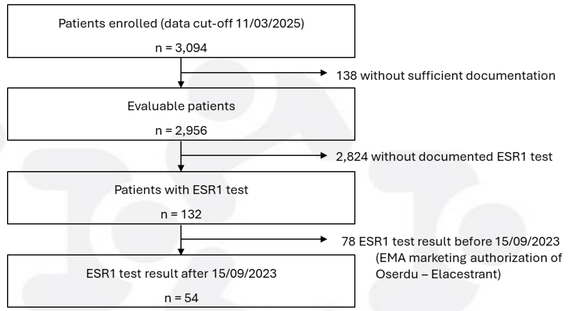
Patients and methods

The AGMT_MBC-Registry is a multicenter nationwide ongoing retrospective and prospective registry for MBC patients in Austria.

Inclusion criteria for this analysis:

- sufficient data quality
- ESR1 mutation testing after the approval of elacestrant in Austria

Figure 1. *Consort diagram.*



Results

As of March 11, 2025, the registry included 3,094 patients, of whom 2,956 were evaluable. Among these, 132 patients (4.5%) had documented ESR1 testing. A total of 59 tests were performed in 54 patients after the approval of elacestrant (**Figure 1**). Detailed patient characteristics are provided in **Table 1**.

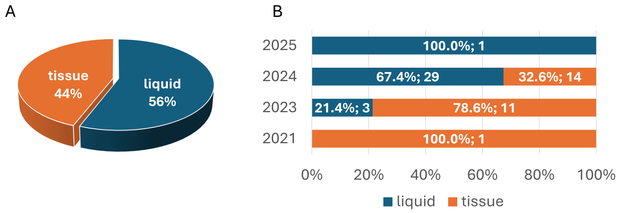
Table 1. *Characteristics of patients with ESR1 testing (n = 54)*

Median age (min-max) *	62 (39-82)
Stage at first diagnosis	
stage I-III	35 (64.8%)
stage IV (*de novo* metastatic)	19 (35.2%)
Menopausal status *	
postmenopausal	37 (77.1%)
premenopausal	11 (22.9%)
unknown	6
Metastatic sites *	
visceral disease	20 (37.0%)
non-visceral disease only	33 (61.1%)
Median number of metastatic sites (min-max) *	2 (1.0-5)
Number of metastatic sites *	
1	27 (50.0%)
2	16 (29.6%)
3+	11 (20.4%)
Receptor status	
HR+/HER2-	48 (92.3%)
HR+/HER2+	1 (1.9%)
HR-/HER2+	2 (3.8%)
Triple-negative (TNBC)	1 (1.9%)
missing	2
Grade	
1	1 (2.4%)
2	20 (48.8%)
3	20 (48.8%)
unknown	13
Disease-free survival (DFS; stage I-III)	n= 35
DFS < 24 months	4 (12.5%)
DFS ≥ 24 months	28 (87.5%)
not evaluable	3

* at diagnosis of metastatic disease

Liquid biopsy vs. tissue analysis

Figure 2. *More than half of the tests were performed as ctDNA tests (A) with an increasing percentage over the years (B).*



ESR1 positivity rate

Table 2. *Test results per test and per patient.*

	Number of tests N=59	Number of patients N=54
ESR1 mutated	17 (**30.4%**)	14 (**27.5%**)
1 ESR1 mutation	15 (26.8%)	11 (21.6%)
2 ESR1 mutations	1 (1.8%)	2 (3.9%)
3 ESR1 mutations	1 (1.8%)	1 (2.0%)
ESR1 not mutated	39 (69.6%)	38 (74.5%)
No result or unknown	3	3

Type of ESR1 mutation and distribution pattern

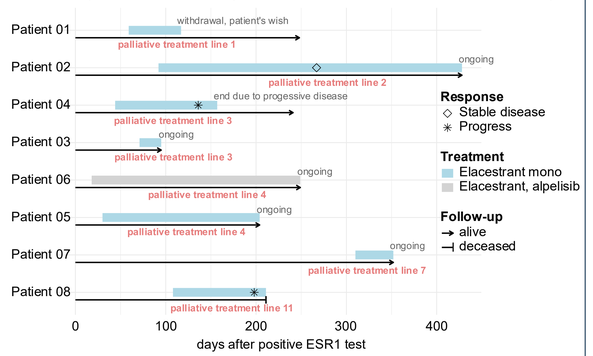
Table 3. *All ESR1 mutations were located in the ligand binding domain.*

ESR1 mutation	Exon	Number of tests N=20*	Number of patients N=14*
D538G	8	5	5
E380Q	5	5	5
Y537S	8	5	4
Y537N	8	3	2
M396V	6	1	1
L536_D538>P	8	1	1

* one patient could have more than one mutation, one test can display more than one mutation

Elacestrant use and treatment response

Figure 3. *Details of all 8 patients with ESR1 mutation and elacestrant treatment (timeline from first positive ESR1 test to last contact shown).*



Co-mutations with PIK3CA, TP53 and BRCA1/2

Table 4. *11 (78.5%) of patients with ESR1 mutation had co-mutations.*

	Testing for co-mutations performed	Co-mutation found
PIK3CA	11 (78.5%)	7 (**63.6%**)
TP53	8 (57.1%)	3 (**37.5%**)
BRCA1/2	9 (64.3%)	1 (11.1%)

Conclusion

This real-world data highlights the clinical relevance of ESR1 mutations in HR+/HER2- metastatic breast cancer patients and underscores the potential impact of molecular-guided treatment. The association of ESR1 mutations with co-mutations in PIK3CA, TP53, and BRCA1/2 suggests the need for personalized treatment approaches.

Funding: The registry is supported by grants from Roche, Daiichi Sankyo, Novartis, Pfizer, Caris Life, Sciences, Lilly, Seagen, Gilead, Astra Zeneca, Stemline Therapeutics, MSD, Agendia, Celgene, AOP Orphan, Sirius Medical, Merck, Takeda, Amgen, BMS, Sandoz. Janssen, GlaxoSmithKline, Menarini, Pierre Fabre, Bayer, Myriad, Delphi Diagnostics

Conflicts of Interest: **Employment or Leadership Position:** None; **Consultant or Advisory Role:** S.P.G., V. C., R.B., G.R., R.P., C.D., C.S., S.H., L.S., M.S., T.W., A.F.Z., C.A.S., D.E., P.P-I., F.R., J.A., K.S-W., R.B., M.H., M.K., R.G.; **Stock Ownership:** R.G.; **Honoraria:** S.P.G., V. C., R.B., G.R., R.P., C.D., C.S., S.H., L.S., M.S., T.W., A.F.Z., D.E., F.R., K.S-W., R.B., M.H., C.F.S., R.G.; **Contracted Research:** S.P.G., R.B., M.S., S.H., D.E., L.S., M.K., C.F.S., R.G.; **Other (e.g. traveling support):** S.P.G., V.C., G.R., R.B., A.P., W.H., R.P., C.D., S.H., L.S., M.S., T.W., A.F.Z., D.E., C.A.S., C.H., P.P-I., F.R., V.C., M.H., C.F.S., R.G.

This poster is the intellectual property of Simon P. Gampenrieder. Contact s.gampenrieder@salk.at for permission to reprint and/or distribute.