

Table of Contents

1 Introduction6

1.1 Epidemiology Worldwide and in Switzerland6

1.2 Breast Cancer Subtypes7

1.2.1 Hormone Receptors7

1.2.2 HER28

1.2.3 Ki-67 and Grading8

1.2.4 Gene Profiling and Pathology.....9

1.2.5 Summary of Subtypes9

1.3 Hormone-receptor Negative Breast Cancer.....11

1.3.1 HER-2 Positive Breast Cancer11

1.3.2 Basal-Like and Triple-Negative Breast Cancers11

1.3.2.1 Basal-Like Breast Cancer12

1.3.2.2 Defining Triple Negativity12

1.3.2.3 Characteristics13

1.4 Discordance in Receptor Status14

1.5 Metastatic Breast Cancer14

1.5.1 Therapy.....15

1.6 Objectives17

2 Patients and Methods.....18

2.1 Setting.....18

2.2 Patients.....18

2.3 Definitions21

2.4 Subtypes23

2.5 Advanced Breast Cancer25

2.6 Discordance in Receptor Status25

2.7 Statistics26

2.8 Survival analysis26

2.9 Ethics Committee Approval26

3 Results.....27

3.1 Data27

3.2 Patient Population27

3.3 Tumor Characteristics and Subtypes.....27

3.4 Hormone-insensitive Breast Cancer28

3.5 Local Recurrence32

3.6 Sites of Metastases32

3.7 Hormone-receptor and HER2 discordance between primary site and relapse site .34

3.8 Therapies34

3.9 Survival36

3.9.1 Survival according to hormonal subtype in patients with HER2 positive vs. HER negative breast cancer38

3.9.2 Survival in the Elderly.....40

3.9.3 Multivariate Analysis40

4 Discussion.....42

4.1 Data42

4.2 Patients.....42

4.3 Subtypes43

4.4 Hormone-insensitive Breast Cancer43

4.4.1 Time to Metastasis and Survival.....43

4.4.2 Patterns of Metastasis.....44

4.4.3 Triple Negative Breast Cancer45

4.5 Infiltrating Lobular Carcinoma.....45

4.6 HER2-positive Breast Cancer.....46

4.7 Local Recurrence46

4.8 ER, PgR and HER2-Receptor Discordance between Primary Breast Cancer and Metastases47

4.9 Therapy.....48

4.10 Limitations and Strengths.....48

4.11 Conclusion49

5 Funding.....50

6 Disclosure of Potential Conflict of Interest50

7 Acknowledgements51

8 Declaration of Authenticity.....52

9 Appendix53

10 Alphabetisches Abkürzungsverzeichnis:54

11 References55