Abraxane (Nab-Paclitaxel):

The Phase II SNAP trial was designed to evaluate the efficacy of alternative chemotherapy schedules for prolonged administration in HER2-negative metastatic breast cancer (MBC), after a short induction at conventional doses. Between April 2013 and August 2015, 258 women untreated with chemotherapy for their HER2-MBC were randomly assigned to receive three different maintenance chemotherapy schedules after three cycles of identical induction chemotherapy: Arm A, nab-paclitaxel 150 mg/m² days 1 and 15 Q28; Arm B, nab-paclitaxel 100 mg/m² days 1, 8 and 15 Q28; Arm C, nab-paclitaxel 75 mg/m² days 1, 8, 15 and 22 Q28. Induction was three cycles nab-paclitaxel 150/125 mg/m², days 1, 8 and 15 Q28. The primary objective was to evaluate the efficacy of each maintenance schedule in terms of progression-free survival (PFS) as compared with the historical reference of 7-month median PFS reported by previous studies with first-line docetaxel. Median PFS in Arm A was 7.9 months; Arm B was 9.0 months, and Arm C was 8.5 months. Grade ≥2 sensory neuropathy was reported in 37.9%, 36.1% and 31.2% of the patients in arm A, B and C, respectively. [https://www.ncbi.nlm.nih.gov/pubmed/29228091/?i=5&from=/26712590/related]

Afinitor (Everolimus) – Two Studies:

MBC patients treated with the combination of everolimus and exemestane at Moffitt Cancer Center were subdivided into 3 groups: 77 patients were started on 10mg daily, 29 patients were started on 7.5mg daily, and 31 patients were started on 5mg daily. There was no significant difference in PFS between starting the recommended dose or a lower dose. Patients initiated on lower doses were less likely to require dose reductions or discontinue due to toxicity, even with later dose increases. If oncologists are more comfortable starting a lower dose, survival may not be adversely affected and patients may be more compliant, deriving a prolonged benefit from the combination. [https://ascopubs.org/doi/abs/10.1200/JCO.2016.34.15_suppl.e12058]

Ibrance (Palbociclib):

A Phase II study that randomized 72 HR+ HER2- MBC patients to receive Ibrance in either a 125 mg or 100 mg dose in combination with physician’s choice of fulvestrant or tamoxifen concluded that the 100 mg dose was associated with a lower rate of grade 3 or 4 neutropenia. Furthermore, both Progression Free Survival and clinical benefit were the same in both groups. Dr Hope Rugo was the lead investigator. [https://www.targetedonc.com/news/reduced-palbociclib-dose-associated-with-lower-rate-of-neutropenia-in-hr-metastatic-breast-cancer]

Kisqali (Ribociclib): As per SABCS 2018 Poster P6-18-06: Conclusion: “The results from across the MONALEESA program suggest that the efficacy of ribociclib was maintained regardless of dose intensity.”

Xeloda (Capecitabine) – Two Studies:

An analysis of dose modification and outcomes from four Phase II capecitabine monotherapy trials, one Phase III capecitabine/docetaxel combination trial, and an analysis of consecutive MBC patients who received capecitabine outside of a clinical trial concluded that reduced capecitabine doses were associated with a lower incidence of treatment-related adverse events, specifically hand-foot syndrome, diarrhea, and stomatitis. Furthermore, time to disease progression and overall survival were similar, or even slightly longer, among patients who received lower vs. full-dose capecitabine in all of the studies reviewed. [https://www.clinical-breast-cancer.com/article/S1526-8209(11)00111-X/fulltext]

At the University of Southern California (USC) hospitals, capecitabine is routinely prescribed at dosages as low as 600 mg/m² twice daily, with a majority of MBC patients receiving a flat dosage (not adjusted for BSA) of 1000 mg twice daily. In a review of 84 patients who received a median capecitabine dosage of 565 mg/m² twice daily, the median PFS among the 62 patients with measurable disease was 4.1 months, which was similar to the median PFS values (4.4 months; 4.2 months) for single agent capecitabine reported in the two major trials with similar eligibility criteria. Furthermore, only 2 patients (2.4%) discontinued capecitabine due to toxicity, supporting our hypothesis that starting treatment at low dosages minimizes side effects while preserving efficacy. [https://www.gotoper.com/publications/ajho/2015/2015feb/efficacy-of-very-low-dose-capecitabine-in-metastatic-breast-cancer]

*There is one instance we’re aware of whereby an MBC drug (Fulvestrant/Faslodex) had an **increase in dosage** due to improved efficacy at the **higher dose**: Median OS was 26.4 months for Fulvestrant 500mg vs. 22.3 months for 250mg. [https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3906991/]

Non-Inferiority of Reduced Drug Dosages*

[https://www.ncbi.nlm.nih.gov/pubmed/2]

Abnormalities in HER2