Conclusions: This study first retrospectively analyze the value of pyrotinib in the era of dual anti-HER2 therapy, preliminarily showing good efficacy and safety of pyrotinib in patients after prior trastuzumab and pertuzumab.

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454P Real-world genomic profiling of patients with advanced or metastatic triple-negative breast cancer in the UK and EU4: A systematic literature review

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Background: Advanced or metastatic triple-negative breast cancer (A/M TNBC) is a detrimental disease with limited treatment options. Molecular subtyping of A/M TNBC has the potential to enhance diagnostic accuracy and further enable targeted therapies, given its high degree of heterogeneity. This systematic literature review (SLR) aimed to identify real-world evidence for genetic alterations among A/M TNBC patients.

Methods: Key biomedical databases (EMBASE®, MEDLINE®, MEDLINE-in-process) were searched to identify real-world studies assessing genomic alterations among A/M TNBC patients in the UK and EU4. The current review followed a standard HTA compliant two review process methodology for screening and data extraction.

Results: A total of three of 203 studies fulfilled the inclusion criteria. All three studies were conference proceedings, with one study each conducted in Spain, Italy, and the UK. A total of 399 A/M TNBC patients were analyzed for genetic profiling across these studies, using either digital droplet PCR (ddPCR), error-corrected 73-gene targeted panel (Guardant360), or AVENIO Expanded ctDNA Analysis Kit. In the Gruppo Italiano Mammella 14 BIOMETA study, BRCAmu+ was detected among 8% of 195 mTNBC patients. Further, in the RegistEM study, 50% of 32 Spanish mTNBC patients had TP53mu+, followed by MAP2K1mu+ and APCmu+ (25% each). In the UK plasmaMATCH study, PIK3CA mutation was more prevalent (9.3% and 14.7% by ddPCR and targeted ctDNA panel, respectively), while ESR1mu+ was the least prevalent (0% and 0.7% by ddPCR and targeted ctDNA panel, respectively). The targeted ctDNA sequencing identified definite genomic profiles compared to ddPCR.

Conclusions: The current SLR highlights the scarcity of real-world evidence on genetic alterations in A/M TNBC. Molecular subtyping exhibits a significant potential in identifying specific genetic alterations, emphasizing the need for further research and larger-scale studies.

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455P Post progression treatments after endocrine therapy (ET) plus palbociclib in patients with HR+/HER2- metastatic breast cancer (MBC): A prospective, real-world study

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Background: The association of ET and CDK 4/6 inhibitors (CDK 4/6i) is the gold standard of treatment in women with HR+/HER2- MBC. The optimal therapeutic strategy after CDK 4/6i progression is still a matter of debate. The present study aimed to evaluate the benefit of the different treatments adopted in a real-world context.

Methods: In this prospective study we included women with HR+/HER2- MBC progressing to ET plus palbociclib (P). Either ET or chemotherapy (CT) were prescribed taking into account:1) site and burden of disease (visceral/plurimetastatic *vs* bone only/oligometastatic); 2) median PFS1 (<4 months *vs* ≥4 months); 3) tolerability profile; 4) patient's preferences. Primary objective was median progression-free survival 2 (PFS2). Secondary aims: analysis of the determinants of physician's choice, clinical benefit rate (CBR), impact of neutrophil-to lymphocyte ratio (NLR), monocyte-to lymphocyte ratio (MLR), platelet-to lymphocyte ratio (PLR) and body mass index (BMI) on PFS2.

Results: From May 2017 to October 2021, 78 pre- and postmenopausal patients were enrolled and 56 were evaluable for the final analysis: 18 had received ET plus P as 1st line, 38 in ≥2nd line; 22 patients were excluded because they were still on therapy at the time of the last follow-up. At progression 15 patients (26.7%) received ET (everolimus+exemestane 8, fulvestrant 7) and 41 (73.2%) were treated with CT (eribulin, capecitabine, nab-paclitaxel, vinorelbine). In the whole population mPFS1 was 17.5 months; mPFS2 was 5 months in the overall cohort (95% CI = 4-48 months) with a significant difference between ET and CT (10 months *vs* 5 months, p=0.035); CBR was 50% and 55.2%, in ET and CT, respectively. At multivariate analysis CT prescription was associated to a higher visceral burden and a shorter mPFS1. Elevated NLR and PLR were correlated with worse PFS2 in both treatment groups, while no impact of MLR and BMI was observed.

Conclusions: In this real life experience, treatments beyond ET plus P failure provided limited but comparable clinical benefit. The physician's choice was clearly driven by visceral burden of disease; the inflammatory status seems to have a detrimental effect on PFS2.

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456P Quality of life (QOL) analysis from the phase II RIGHT choice study of first-line ribociclib (RIB) + endocrine therapy (ET) vs combination chemotherapy (combo CT) in aggressive HR+/HER2− advanced breast cancer (ABC)

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Background: RIGHT Choice showed a statistically significant median progression-free survival benefit of ≈1 yr with first-line RIB + ET vs combo CT (HR, 0.54; P=0.0007) in patients (pts) with aggressive HR+/HER2− ABC. As QOL data provide information on real-life treatment (tx) benefit as well as impact tx choice and duration, a QOL analysis was performed.

Methods: Pre/perimenopausal pts with no prior systemic therapy for aggressive HR+/HER2− ABC were randomized 1:1 to RIB + ET or combo CT. The FACT-B scores were determined by a questionnaire administered at protocol-defined time points. The median time to deterioration (mTTD) in overall health status, nausea or pain was defined as a composite endpoint of time from randomization to either first occurrence of ≥10% deterioration in FACT-B scores with no later improvement or date of discontinuation due to progressive disease, death, or adverse events. Only pts with baseline and at least one post-baseline pt reported outcome assessment were included. Pts without events were censored at the last evaluation prior to the earliest of cutoff date, end of tx, start of new tx, or when lost to follow-up, or at consent withdrawal. Descriptive summary of change from baseline in FACT-B total score was also summarized.

Results: The composite endpoint of mTTD in overall health status was delayed with RIB + ET (N=111) vs combo CT (N=96;16.8 vs 10.6 mo; HR, 0.63; Table). The mTTD in subdomains of nausea (18.4 vs 10.4 mo; HR, 0.56) and pain (13.0 vs 10.4 mo; HR, 0.70) was also delayed in pts on RIB + ET vs combo CT. A numerical trend in change from baseline in FACT-B total scores during tx favoring RIB + ET over combo CT was observed.

Table: 456P

End Points	Outcomes	RIB + ET (N=111)	Combo CT (N=96)
TTD in overall health status	**Deterioration events, n**	67	66
	FACT-B score decrease, n_1/n (%)	24/67 (35.8)	22/66 (33.3)
	Tx discontinuation, n_2/n (%)	43/67 (64.2)	44/66 (66.7)
	mTTD, mo	16.8	10.6
	HR; 95% CI	0.63; 0.44-0.90	
TTD in nausea	**Deterioration events, n**	67	69
	FACT-B score decrease, n_1/n (%)	29/67 (43.2)	30/69 (43.5)
	Tx discontinuation, n_2/n (%)	38/67 (56.7)	39/69 (56.5)
	mTTD, mo	18.4	10.4
	HR; 95% CI	0.56; 0.39-0.79	
TTD in pain	**Deterioration events, n**	72	65
	FACT-B score decrease, n_1/n (%)	34/72 (47.2)	22/65 (33.8)
	Tx discontinuation, n_2/n (%)	38/72 (52.8)	43/65 (66.2)
	mTTD, mo	13.0	10.4
	HR; 95% CI	0.70; 0.49-0.99	

Conclusions: This analysis suggests that first-line RIB + ET is associated with better QOL than combo CT for pts with aggressive HR+/HER2− ABC, providing supportive evidence for RIB + ET use in this pt population.

Clinical trial identification: NCT03839823.

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457P Disparities in receipt of CDK4/6 inhibitors with endocrine therapy as therapy for hormone receptor-positive, HER2-negative metastatic breast cancer in the real-world setting

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Background: This retrospective study, using real-world evidence (RWE), compared outcomes for patients receiving treatment for hormone receptor-positive (ER+), HER2-negative, metastatic breast cancer (MBC) with CDK4/6 inhibitors (CDK4/6i) in combination with endocrine therapy (ET) versus ET alone and explored disparities in use of CDK4/6i.

Methods: We used the nationwide electronic health record-derived Flatiron Health de-identified database to examine real-world impacts of CDK4/6i and ET. A total of 3,917 patients received CDK 4/6i+ET (n=2170) or ET alone (n=1747) in the first-line setting between February 2015, and November 2021. Characteristics of patients receiving CDK4/6i+ET versus ET alone were compared using statistical tests. Baseline characteristics were balanced using inverse probability weighting (IPW). Kaplan-Meier method and Cox proportional hazards were used to test the impact of CDK4/6 treatment on rwPFS and rwOS.

Results: Compared to patients receiving ET alone, those received CDK4/6i+ET were younger, more likely to have presented with de novo MBC (36% vs. 29%, p<0.001), had better performance status (50% vs. 40% patients with ECOG value 0, p=0.001), and more likely to have lower number of comorbidities (30% vs. 27% with at least 1 comorbidity, p=0.04). After IPW adjustment, CDK4/6i+ET treatment was associated with significantly longer median PFS compared to ET alone (27 vs 17 months; hazard ratio [HR]=0.61, p<0.001). Median OS was 52 months in the CDK4/6i+ET group and was 42 months with ET alone (HR=0.74, p<0.001).

Conclusions: RWE confirms the added PFS and OS benefit of adding CDK4/6i to endocrine therapy in patients with ER+, HER2-negative MBC. We found disparities in CDK4/6i use by age, stage at diagnosis, baseline Ecog value, and number of comorbidities. Future work is needed to improve access to this important class of drugs.

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458P Metastatic breast cancer: How and how often do we communicate? Results from an Italian national survey

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Background: Communication is a complex process; an effective communication requires a two-way relationship between patients (pts) and healthcare providers (hp). The areas of communication concern diagnosis, prognosis and treatment. In this context, a tailored communication approach is suggested to keep pts involved in the clinical decision-making process.

Methods: Between 21 June and 4 October 2022, a 38-question web survey, promoted by the IncontraDonna Foundation and carried out in collaboration with both the Italian Society of Psycho-Oncology (SIPO) and the Italian Association of Medical Oncology (AIOM), was sent to oncologists members of AIOM. The aim of this study was both to investigate how and how much oncologists communicate with metastatic breast cancer pts (mBCp) and to probe clinicians' opinions and needs.

Results: 140 oncologists from 19 Italian regions participated in the survey. Responders reported discussing prognosis with their mBCp both in terms of residual life (96%), goals of care (98%) and likelihood of treatment response (94%), in the last two cases especially at the time of the first oncological visit (67% and 60%, respectively). As many as 93% of responders stated that they investigate the degree of understanding of the information provided. In communicating the prognosis, 49% of responders considered the presence of a caregiver "very useful" and 61% considered her/his absence "very disadvantageous". About the organization of one's department, the time dedicated to doctor-patient communication was considered "quite sufficient" in 16%", "little but sufficient" in 44%, "scarce" in 31% and "insufficient " in 10% of cases. In 89% of cases the presence of a psycho-oncology service was reported, to which mBCp would be referred regularly in only 14% of cases. Specific training courses for hp (69%) and periodic meetings with expert psycho-oncologists (59%) are the improvement actions most requested by clinicians.

Conclusions: The results of this survey highlighted heterogeneity in the management of communication in mBCp across the Italian country. Although the figure of the psycho-oncologist is considered important, its integration into the therapeutic process still appears complex.

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