NCCN Request for Proposals (RFP): Elucidating Biomarkers and Mechanisms of Resistance to CDK 4 and 6 inhibitors Through Preclinical, Clinical, and Real World Evidence Studies of Abemaciclib for Breast Cancers

1.0 Purpose

The National Comprehensive Cancer Network (NCCN) has received a Two Million Dollar research grant from Eli Lilly and Company (hereafter, “Grantor”) to support the performance of preclinical, real world evidence (RWE), clinical and correlative studies of abemaciclib in the treatment of breast cancer aimed at elucidating and overcoming de novo and acquired resistance to CDK 4 & 6 inhibitors. NCCN will serve as the funding organization. Grants are available only to investigators from NCCN Member Institutions.

The original RFP, issued on January 25, 2019, called for the design and performance of preclinical, clinical, and correlative studies using abemaciclib to treat breast cancer. It was well received and two innovative pre-clinical studies were selected for funding. The scope has been broadened and funds are still available to support the performance of preclinical, real world evidence, clinical and correlative studies of abemaciclib in the treatment of breast cancer aimed at elucidating and overcoming de novo and acquired resistance to CDK 4 & 6 inhibitors.

2.0 Scope and Aims

NCCN has received a grant from the Grantor for the design and performance of preclinical, RWE, clinical, and correlative studies using abemaciclib to treat breast cancer.

CDK 4 & 6 inhibitors have improved progression-free survival (PFS), overall response rate (ORR), and survival outcomes in patients with HR+, HER2- advanced breast cancer (ABC), both as initial therapy and after progression on endocrine therapy (ET). Currently, there are three FDA-approved CDK 4 & 6 inhibitors (palbociclib, ribociclib, and abemaciclib). Despite this positive clinical outcome, not all patients benefit from CDK 4 & 6 inhibitors and a significant number of patients eventually have disease progression, underscoring the need to elucidate the mechanisms of resistance and inform development of novel therapeutic combinations that circumvent this resistance.

The overall aim is to develop innovative research in the area of resistance to CDK 4 & 6 inhibitors in order to discover predictive markers and develop novel rational combination therapies by improving medical knowledge and clinical use of this class of therapeutics. Proposals (which can be preclinical/translational, RWE, phase I/II clinical trials or correlative trials) submitted in response to this RFP will be useful in guiding further development of abemaciclib and novel rational combination therapies to overcome resistance to CDK 4 & 6 inhibitors.

Proposals for research projects which address one of the following focus areas are highly desired:

Focus 1: Preclinical/Translational Research
Preclinical/translational studies focused on characterizing mechanisms of resistance from patient samples. Preference will be given to studies that specifically addresses the following:
• Defining the molecular alterations underlying de novo and/or acquired resistance to CDK 4 & 6 inhibitors in combination with endocrine therapy, in patient samples.
• Determining the extent to which resistance to monotherapy abemaciclib differs from resistance to CDK 4 & 6 inhibitors in combination with endocrine therapy.
• Mechanistic validation of the molecular alterations identified in tumors progressing on CDK 4 & 6 inhibitor therapy that confer resistance in preclinical models.
• Evaluating rational combination therapy based on the genomic alterations identified from clinical samples in patient derived models of resistance (including organoids and PDXs).

Focus 2: Clinical Trials
Clinical studies that seek to identify and validate biomarkers and mechanisms of de novo and/or acquired resistance or those that focus on post-CDK 4 & 6 inhibitor therapy for HR+ metastatic breast cancer with preference for the following:
• Rational novel combination therapies to circumvent resistance based on genomic profiling of breast tumors with de novo and acquired resistance to CDK 4 & 6 inhibitors ± endocrine therapy.
• Proposed trials of abemaciclib (either alone or in combination) post any prior CDK 4 & 6 inhibitor therapy must include a biological enrichment strategy based on a novel molecular marker. Trials investigating sequencing of CDK 4 & 6 inhibitor therapy without this statistical approach will be considered out of scope.
• Clinical studies assessing biomarkers predictive of response to CDK 4 & 6 inhibitors.

The following would be of high impact: incorporation of a correlative/biomarker component into the proposed clinical study using paired biopsy samples (e.g. pre- and post-treatment), liquid biopsy, or PK/PD biomarkers to explore potential mechanism of action, as well as sensitivity and resistance mechanisms. Please refer to Section 10 References (Wonder, et al).

Focus 3: Real World Evidence
RWE is the clinical evidence regarding the usage and potential benefits or risks of a medical product derived from analysis of real world data. Real-world data (RWD) are the data relating to patient health status and/or the delivery of health care routinely collected from a variety of sources and can be collected either retrospectively and/or prospectively. RWD can come from different sources including:
• Electronic health records (EHRs)
• Claims and billing activities
• Product and disease registries

RWE studies (either retrospective or prospective) that seek to identify mechanisms of de novo and/or acquired resistance to CDK 4 & 6 inhibitor therapy, as well as associated sequences of systemic treatment and outcomes are of primary interest. Alteration data generated from paired biopsies both before and after CDK 4 & 6 inhibitor treatment is of strong interest.
All patients included in a retrospective or prospective cohort must have received abemaciclib or be eligible for receiving abemaciclib treatment.

**For clinical trial proposals:**
- All proposed clinical trials (phase I or II; please note that phase III trial proposals are not allowed) must contain abemaciclib.
- Abemaciclib can be combined with investigational and FDA-approved drugs from other pharmaceutical companies or FDA-approved drugs from Lilly (non-FDA approved drugs from Lilly’s pipeline will not be allowed).
- Clinical trials must utilize dosages and dosing schedule based on already known safety data for the drug. Specifically, as a single agent, the starting dose of abemaciclib should be the approved dose of 200 mg PO BID. In combination, the starting dose of 150 mg PO BID abemaciclib should be used and dose reduction per the label, if necessary.

**For preclinical proposals:**
- Lilly will provide drugs in their pipeline (including non-FDA approved drugs) based on material availability. The potential drugs are listed below and may be expanded or retracted based on decisions at Lilly:

<table>
<thead>
<tr>
<th>Early Phase</th>
<th>Aurora Kinase A inhibitor</th>
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<tr>
<td>Late Phase</td>
<td>ramucirumab, abemaciclib</td>
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**For translational/ correlative trial proposals:**
- May be added to an ongoing project or clinical trial

**While a wide variety of proposals are encouraged, the areas of research emphasis for this RFP include:**
- Mechanisms of resistance to CDK 4 & 6 inhibitors. For example (but not restricted to):
  - Resistance to CDK 4 & 6 inhibitors in Rb proficient tumors
  - In HR+ breast cancers, is tumor progression post endocrine therapy + CDK 4 and 6 inhibitors related to endocrine therapy, CDK 4 & 6 inhibitor or both?
  - Difference between acquired and de novo resistance
  - Resistance gene signatures
  - Novel models for CDK 4 & 6 inhibitor resistance (e.g., organoids, patient-derived xenografts)
- Therapy optimization. For example (but not restricted to):
  - Are there differences between CDK 4 & 6 inhibitors in preclinical models?
  - Biomarkers of response and resistance (better patient selection; analysis of extreme responders and progressors; etc.)
  - Novel combinations (synergy/sequencing with PARP inhibitors in BRCA-mutated patients; combinations targeting improvement of apoptotic effect; testing of novel combinations in preclinical models; etc.)
  - Leveraging the immune effects of CDK 4 & 6 inhibitors
- Characterization of mechanisms of toxicity. For example (but not restricted to):
  - Analysis of microbiome and its modulation in GI toxicity from abemaciclib
Specific exclusions from this RFP include:

- No studies will utilize doses outside the range for which safety data is available
- Phase III clinical trial proposals
- Non-FDA approved drugs from Lilly’s pipeline will not be allowed in phase I or II clinical trial proposals (but will be allowed in preclinical proposals)
- Use of other CDK 4 & 6 inhibitors in clinical trials
- Studies that are duplicative of completed, ongoing or planned studies
- Combinations with check-point inhibitors
- Combinations of abemaciclib with everolimus and ET

Collaboration between NCCN Member Institutions is strongly encouraged in order to foster the interactive sharing of knowledge and expertise, and to utilize the combined clinical strengths of members, particularly in the case of uncommon tumors. Although the submitting investigator must be from an NCCN Member Institution, participating institutions do not need to be an NCCN Member Institution. This can also include cross-institutional collaboration for the conduct of correlative studies.

The NCCN Request for Proposals Development Team (RFPDT) developed this RFP with a formalized review procedure to accept applications and select the proposals of highest scientific merit. The NCCN RFPDT oversaw the development of the RFP and a NCCN Scientific Review Committee (SRC) composed of some members of this group will perform the review of applications.

The goal of the RFP is to generate innovative projects that are not duplicative of completed, ongoing or planned studies. A listing of ongoing studies can be found in Section 11.0 of this RFP. If there are any questions about what constitutes duplicative versus complementary research please email Nicole Kamienski at kamienski@nccn.org with the subject line, “2020 Abemaciclib Project”.

3.0 Study Time Frames

All approved clinical studies are expected to commence, which is defined as the first patient receiving the first dose of study drug(s), no later than nine (9) months of notice of study approval and are to complete accrual within two (2) years of commencement. A manuscript must be submitted to NCCN for review no later than nine (9) months after study endpoint achieved. Studies will be funded as described in Section 9.0 and should be designed with subject number commensurate with study time frames and funding.

Studies for rarer cancers or those that require a large numbers of patients for statistical power must be multi-institutional. Network appropriate studies will be considered as long as submitting principal investigator (PI) is from an NCCN Member Institution.

Accepted studies will be held to the following time frames:

Preclinical studies are expected to be completed within a 2-year time frame.

Phase I studies are expected to meet primary objective within 2 years of commencement.
Single-arm Phase II studies are expected to explore new approaches that can be tested in larger confirmatory studies if positive results are obtained. It is expected that these studies will meet the primary objective within 2 years of commencement. To meet this goal, single-arm Phase II trials are encouraged to be multi-institutional. Data management and monitoring of studies should be coordinated by the applying institution. Additional funding for the applying institution may be requested to support the additional resources required for this activity, if the study involves multi-institutional participation.

Randomized Phase II multi-institutional studies are expected to be completed within a 2-year time frame. Multi-institutional data management and monitoring of these studies should be coordinated by the applying institution. Additional funding for the applying institution may be requested to support the additional resources required for this activity.

Real world evidence studies are expected to be completed within a 2-year time frame.

Correlative laboratory studies are expected to be completed within the same time frame as the corresponding clinical trial. Correlative laboratory studies within clinical trials already supported through other mechanisms must be completed within 2 years.

All studies will require documentation of the feasibility of accruing the targeted study population; studies may be multi-institutional.

4.0 Proposals

In order to respond to the RFP, investigators must submit a proposal to NCCN in the format delineated below, which will be evaluated by the SRC.

Proposals are required to be submitted electronically to the NCCN research portal at https://nccn.envisionpharma.com/ienv_nccn and include letters of support from the governing groups of the institution verifying:

1) Office of Sponsored Research approval
2) Department Chair/Division approval
3) Institutional budgetary review and approval
4) Documentation to support feasibility of clinical trials with at least one of the following:
   - Letter from Institution’s Feasibility Committee if applicable
   - Documentation by previous studies and accrual (if available, publications and abstracts
5) Letter(s) of support from participating institutions including name of PI at participating institution and their feasibility

Letters should be addressed to Wui-Jin Koh, MD, CMO, National Comprehensive Cancer Network, 3025 Chemical Road, Suite 100, Plymouth Meeting, PA 19462.

Proposals will provide concise documentation of the research plan. The proposal is expected to contain sufficient information to allow the reviewers to fully assess the scientific rigor of the proposed study. A full research project plan may be submitted as a supplemental attachment. A robust review of the statistical plan will be conducted.
Proposals should contain detailed information regarding the following areas:

4.1 Clinical/Non-Clinical Research/RWE
   A. General Information: Title/Type of Support/Subsite(s)
   B. Investigators and institutional affiliations
   C. Concept information
      i. Enrollment/Design/Phase
      ii. Estimated time of completion
      iii. Overview/Hypothesis
      iv. Background/Rationale
   D. Scientific summary
      i. Primary/Secondary objectives
      ii. Inclusion/Exclusion criteria
      iii. Data source (applicable only to real world data)
      iv. Study population
      v. Anticipated number of abemaciclib patients (applicable only to real world data)
      vi. Statistical analysis
      vii. Treatment plan
      viii. References
   E. Oncology analysis
      i. Tumor Type/Stage
      ii. Correlative study information
      iii. Outcome measures
      iv. Feasibility documentation
   F. Request for product: Formulation Dosage/Quantity
   G. Planned publications: Journal/Congress/Anticipated Dates

4.2 Budget using NCCN template (within iEnvision)
   A. Breakdown by major cost categories
   B. Justification of major costs with enough detail to demonstrate how funding for major elements in the study will be allocated
   C. Salaries are capped at the current NIH salary cap
   D. No travel or publication costs will be covered

4.3 Ancillary Documentation
   A. An NCI format BioSketch of the Principal Investigator
   B. An appendix of supportive literature may be provided

5.0 Proposal Requirements

5.1 Submission

All proposals must be submitted electronically using the directions below and are due on **July 10, 2020 by 11:59 PM (ET)**. No exceptions will be granted.

1. Please use the link below to register in the system:
   [https://nccn.envisionpharma.com/ienv_nccn](https://nccn.envisionpharma.com/ienv_nccn)
2. Select “Register for New Account” in the upper right corner of the page, above the “Log In” button
3. Complete all fields (Note: Fields with an asterisk are required)
4. You will receive a confirmation email. Click on the link in the email to activate your account.
5. Enter your name and password (Note: Your user name is your email address. Do not copy and paste.)
6. Set up your security questions
7. Submit your study
   i. RFP ID: ABEM
   ii. Primary compound: Abemaciclib
8. Refer to “Requestor User Manual” located under the question mark on the upper right side of the screen for additional instructions

For technical assistance with the iEnvision system, please contact iEnvision_general_request@envisionpharmagroup.com.

Studies that have safety issues, are already funded concepts, or are not consistent with the strategy for investigation as written in this RFP will not be reviewed by the SRC.

For questions or issues, please call Nicole Kamienski at (215) 690-0230. NCCN will seek to provide information to potential investigators regarding ongoing or completed studies of abemaciclib in order to avoid the submission of a proposal that is already a studied concept.

5.2 Requirements

5.2.1 Human Biological Specimens: All specimens must be obtained under informed consent and IRB approval appropriate for the study. Compliance with all federal regulations is required.

5.2.2 IRB:

   5.2.2(a) Draft protocols will be reviewed by NCCN and the Grantor prior to IRB review. A copy of the draft protocol must be submitted to NCCN within 4 weeks after the study approval letter. The protocol must be consistent with the approved proposal and all reviewer comments must be addressed.

   5.2.2(b) All investigators will submit protocols for IRB review and document approval to NCCN prior to study activation and all collaborators will furnish evidence of IRB approval. It is expected that IRB review and approval be completed within 150 days following NCCN notification of funding for the project.

5.2.3 IACUC review and approval: All investigators conducting animal experiments will submit research project plans for IACUC review and document approval to NCCN prior to study activation. It is expected that IACUC review and approval be completed within 90 days following NCCN notification of funding for the project.
5.2.4 **Serious Adverse Event Reporting:** All serious adverse events will be reported to NCCN and the Grantor in addition to local regulatory authorities.

5.2.5 **Institutional Monitoring:** All studies will be internally monitored in accordance with appropriate committees (e.g. institutional Data Safety and Monitoring Plan in the case of human studies). A copy of the Data Monitoring Plan for the study must be submitted to NCCN prior to NCCN approval of study activation.

5.2.6 **IND:**

5.2.6(a) Investigators are required to hold INDs for studies but will be allowed to cross-reference a filing to Grantor’s IND. Investigators are encouraged to apply to the FDA for IND exemption if studies meet all criteria according to 21 CFR 312.2(b). A copy of the FDA approval letter for IND exemption must be submitted to NCCN before study drug will be released.

5.2.6(b) If abemaciclib is studied in combination with an investigational agent from another pharmaceutical company, or an agent used outside of its indication, the investigator must provide documentation of that company’s commitment to provide drug for the investigation as well as the agreement of that company to allow presentation and publication of results and allow cross-filing or filing of a new IND. **This documentation must be provided to NCCN along with the proposal.**

5.2.6(c) Proposals using an experimental diagnostic imaging agent that will require an IND must outline how regulatory issues will be handled in order to meet the required study time frame.

5.2.7 **Progress Reports:** Investigators will provide interim progress reports to NCCN detailing the progress of studies quarterly, and upon study completion. These reports will be used administratively for funding purposes. If study progress or accrual lags behind the expected rate, the SRC may be asked for suggestions to improve study progress, or alternatively, to terminate the study and any further funding.

5.2.8 **Specimen Transmittal:** If specimens are to be transported extramurally for collaborative laboratory studies, all institutional requirements for safety and confidentiality will be met.

5.2.9 **Abstracts and Publications:** Abstracts for presentation at scientific meetings and all publications of study results will be submitted to NCCN and Grantor for review related to protection of company’s intellectual property and confidential information **prior to any submission.** Abstracts must be submitted at least 15 days prior to submission and manuscripts at least 30 days prior to submission. Grantor may delay publication and disclosure of the manuscript or abstract for up to an additional sixty (60) days so as to seek patent protection of intellectual property rights.
5.2.10 NCCN Multi-Institutional Studies: Collaborative studies between NCCN Member Institutions are encouraged. For these studies, the proposal feasibility section should provide information about data management, statistical analysis, and specimen handling issues. Additional funding may be provided for centralized data management and monitoring by the applying institution.

5.2.11 NCCN institutions and investigators will be responsible for conducting all studies in accordance with the applicable research plan, GCP Guidelines, and all applicable laws and regulations. NCCN institutions and investigators will be responsible for all data collection, statistical analysis and safety reporting.

5.2.12 Investigators must provide reasonable assurance that submitted studies will be able to reach completion within the time frames specified in Section 4.0.

5.2.13 Final protocols must be consistent with approved proposals. Funds will be rescinded if there are significant changes without prior NCCN approval. There will be no exceptions.

5.2.14 The PI listed on the protocol must be the same PI listed on the proposal submission unless approved by NCCN.

6.0 Drug Supply

Abemaciclib will be supplied for all approved and funded studies by Grantor.

If abemaciclib is studied in combination with an investigational agent from another pharmaceutical company, or an agent is used outside of its indication, the investigator must provide documentation of that company’s commitment to provide drug for the investigation as well as the agreement of that company to allow presentation and publication of results, and allow cross-filing or filing of a new IND.

If pharmacokinetic studies of investigational agents other than abemaciclib are planned, the investigator must provide documentation of that company’s commitment to or alternative mechanism for performing PK studies for that agent. This documentation must be provided to NCCN along with the proposal.

7.0 Selection Criteria

Proposals will be judged based on the following criteria:

1. Scientific value
2. Research experience of the Principal Investigator
3. Soundness of study design
4. Feasibility including reasonable assurance of achieving intended and full Accrual
5. Budgetary reasonableness
6. Statistics
The Grantor has the ability to reject any study with safety issues or if it is an already studied concept.

8.0 Funding

NCCN and its member institutions have an agreement to include a maximum of 25% indirect costs for trials funded by NCCN. Direct funding will include all costs including investigators’ salaries. For example, $80,000 direct costs and $20,000 indirect costs for a total grant of $100,000. Any funds in excess of the limits stipulated in this section for direct funding will require detailed justification and review.

Preclinical studies will be funded up to a total cost of $100,000, including up to 25% indirect costs.

Phase I and Phase II clinical trials will be funded at a cost of up to $300,000 (total costs including direct costs and 25% indirect costs) per trial. Multi-institutional data management and monitoring of these studies should be coordinated by the applying institution. Up to $100,000 in additional funding for the applying institution may be requested to support the additional resources required for this activity.

Real World Evidence Studies will be funded up to a total cost of $100,000, including up to 25% indirect costs.

The Correlative Laboratory studies section of the clinical trial will be funded up to a total cost of $100,000, including up to 25% indirect costs. Unfunded correlative laboratory studies within clinical trials already supported through other mechanisms will also be considered for support.

Funding should not exceed $500,000. Clinical study maximum $300,000 + correlative study maximum $100,000 + multi-institutional funding maximum $100,000 = $500,000 MAXIMUM funding.

Funding will be disbursed to approved studies as follows:

(a) Research Projects (Basic Research and Real World Evidence):
   - 50% upon approval of Protocol;
   - 35% upon completion of research and receipt of final report by NCCN; and
   - 15% upon submission of article for publication.

(b) Phase I trials:
   - 15% after IRB approval and dosing of first Study Subject;
   - Based on the per Study Subject costs, after the initial 15% of funding has been accounted for based on Study Subject accrual, funds will be awarded on a quarterly basis for eligible Study Subjects enrolled in a Study, based on the per Study...
Subject rate up to a maximum of an additional 65% of the funding; and

- 20% of funds will be awarded after submission of a manuscript for publication.

(c) Phase II trials and correlative Study(ies):

- 15% after IRB approval and dosing of first Study Subject;
- Based on the per Study Subject costs, after the initial 15% of funding has been accounted for based on Study Subject accrual, funds will be awarded on a quarterly basis for eligible Study Subjects enrolled in a Study, based on the per Study Subject rate up to a maximum of an additional 65% of the funding; and
- 20% after submission for publication.

(d) Phase II trials with 2-Stage Design with Early Stopping Rules

- 15% of total requested funding (based on maximum number of anticipated Study Subjects) after IRB approval and dosing of first Study Subject;
- Remainder of per Study Subject funding for the number of Study Subjects in the first stage after all Study Subjects are accrued to the first stage of a Study (total funding for the number of Study Subjects in first stage less the initial payment) up to a maximum of an additional 65% of the funding;
- Total per Study Subject funding for the number of Study Subjects in the second stage less final payment after all Study Subjects are accrued to the second stage; and
- 20% of total requested funding (based on maximum number of anticipated Study Subjects) after submission of a manuscript for publication or of a final report.

(e) Multi-center Randomized Phase II Study(ies):

- 15% after IRB approval and dosing of first Study Subject;
- Based on the per Study Subject costs, after the initial 15% of funding has been accounted for based on Study Subject accrual, funds will be awarded on a quarterly basis for eligible Study Subjects enrolled in a Study, based on the per Study Subject rate up to a maximum of an additional 65% of the funding;
- 20% after submission for publication; and
- Any additional funding will be disbursed to the coordinating center for data management and monitoring. These funds will be delegated at the discretion of the lead Principal Investigator.
and may include outsourcing of data management and/or monitoring to an independent research organization.

The goal is to have rapid submission of a manuscript so as to have the data available to the wider scientific community.

**Studies that do not meet the time frame requirements as stipulated in Section 4.0 will have funds rescinded and will be required to return any and all unused funds previously disbursed.**

### 9.0 Study Agreement

A study agreement will be signed between NCCN and each awarded institution.

If an institution requires a separate contract with another pharmaceutical company for a study, that contract must be fully executed by the time of final contract execution with NCCN.

All aforementioned points between NCCN and the participating institution must be strictly adhered to.

### 10.0 References


### 11.0 Ongoing Research Projects

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<thead>
<tr>
<th>TREATMENT</th>
<th>TUMOR TYPE</th>
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<tbody>
<tr>
<td>Neo-Adjuvant</td>
<td></td>
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<tr>
<td>Abema</td>
<td>Surgically Resectable, Chemo Resistant TNBC</td>
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<tr>
<td>Abema + Trastuz +</td>
<td>ER+, HER2+ BC</td>
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<tr>
<td>Paclitaxel + Fulvestrant</td>
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<tr>
<td>Abema</td>
<td>HR+, any HER2 status</td>
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<tr>
<td>Combination</td>
<td>Description</td>
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<td>-----------------------------</td>
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<tr>
<td>Abema + Fulvestrant</td>
<td>HR+, recurrence on adjuvant Endo tx. Salvage Surgery</td>
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<tr>
<td>Abema + Aromatase Inhibitors</td>
<td>HR+ BC (window)</td>
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<td>Abema + Niraparib</td>
<td>HR+ BC</td>
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<td>Abema + SOC</td>
<td>Pre-op HR+ early BC</td>
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<tr>
<td>Abema + Anastrozole+ Venetoclax</td>
<td>ER+ HER2- BC</td>
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<td>Abema + Letrozole vs Chemo</td>
<td>Luminal BC</td>
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**Adjuvant**

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<th>Description</th>
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<tr>
<td>Abema + Hydroxychloroquine</td>
<td>EBC</td>
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<tr>
<td>Abema</td>
<td>ctDNA HR+ HER2-</td>
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<tr>
<td>Abema + ET vs ET</td>
<td>HR+ HER2-</td>
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**Metastatic**

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<tbody>
<tr>
<td>Abema + Aromatase Inhibitors</td>
<td>HR+ HER2- 2nd line MBC post fulv</td>
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<tr>
<td>Abema + Fulvestrant &amp;/or Trastuz</td>
<td>Brain mets</td>
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<td>Abema + Fulvestrant</td>
<td>&gt;70 yrs age MBC</td>
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<td>Abema + ET</td>
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<td>Abema</td>
<td>ILD in MBC</td>
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<td>Abema + Letrozole +/- Pertuzumab</td>
<td>ABC</td>
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<tr>
<td>Abema</td>
<td>RWE (quality of life assessments)</td>
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<td>Abema + Tucatinib</td>
<td>HER2+ MBC</td>
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<td>Abema + Fulvestrant vs Abema</td>
<td>HR+, HER2- MBC</td>
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<td>Abema + T-DM1</td>
<td>HER2+ MBC</td>
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<td>Abema</td>
<td>RB+ TNBC</td>
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<td>Abema + Aromatase Inhibitors</td>
<td>HR+ HER2– second line; MBC– post Fulvestrant</td>
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<td>Abema + HCQ</td>
<td>HR ER+</td>
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<td>Abema + Bicalutamide</td>
<td>HR+, HER2-, MBC</td>
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<td>Abema + ET</td>
<td>HR+ Her2- First line MBC (visceral met) vs Chemo</td>
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<td>HR+ Her2</td>
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<td>Abema + Endocrine</td>
<td>Symptomatic MBC</td>
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<td>Abema + probiotics+ SOC (diarrhea study)</td>
<td>ER+/HER2- MBC</td>
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<td>abema + SERD</td>
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<tr>
<td>Abigail (Abema + Fulvestrant / mBC 1st line)</td>
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<td>Abema + stereotactic radiotherapy</td>
<td>HR+/HER2- mBC</td>
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<td>MORPHEUS (Abema + atezolizumab / mBC)</td>
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<td>HR+/HER2- mBC</td>
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<td>Abema + Bcl-2 inhibitor /mBC</td>
<td>HR+/HER2- mBC</td>
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