Agendia Data Analysis Pipeline Tool (ADAPT-CE)

User Guide

For use only in combination with the MammaPrint® and BluePrint® Breast Cancer Recurrence and Molecular Subtyping Kit

MAMMAPRINT+BLUEPRINT
Illuminating Tumor Biology

EM-002-v6 (2025 March)

Contents

Introduction

This User Guide covers important information on how to use the Agendia Data Analysis Pipeline Tool (ADAPT-CE), which is a high-performance and security-compliant cloud-based genomics analysis platform. ADAPT-CE is intended to be used in combination with the MammaPrint® BluePrint® Breast Cancer Recurrence and Molecular Subtyping Kit (MammaPrint BluePrint Kit). ADAPT-CE delivers integrated analysis and results reporting of samples processed with the MammaPrint BluePrint NGS Kit.

This User Guide will provide step-by-step instructions to create an account, install a secure file connector, upload, and analyze de-identified patient data in a secure environment, and retrieve test results.

Prior to starting, review all the instructions in this User Guide.
If you still have questions after reading this User Guide, please contact NGS.support@agendia.com for assistance.

System Requirements

ADAPT-CE REQUIREMENTS

ADAPT-CE is a secure cloud-based system which can be accessed through the supported browsers listed below.

Browser	Supported Version	Operating System
Google Chrome	Most recent stable version	Windows, Mac, and Linux
Mozilla Firefox	Most recent stable version	Windows, Mac, and Linux

For proper functioning of ADAPT-CE, ensure that cookies are enabled in the browser.

AGENDIA SERVICE CONNECTOR REQUIREMENTS

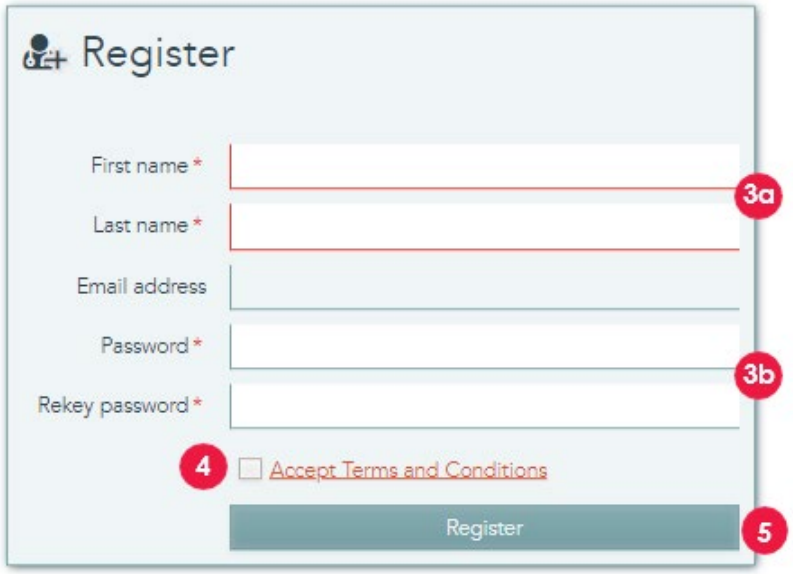
The Agendia Service Connector is a secure file transfer connector that will need to be installed to upload data to ADAPT-CE.

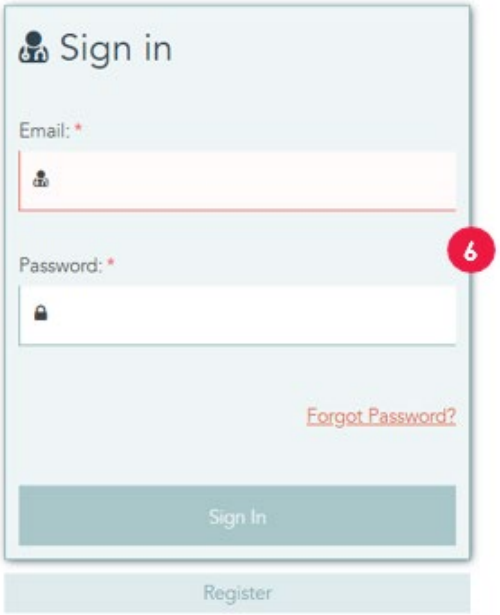
The Agendia Service Connector can be installed in Windows, Mac and Linux environments.

For proper functioning of the connector:

- Ensure that your Internet connection is 1.5 Mbps or faster.
- Ensure the outbound ports TCP443 (SSL) and TCP22 (SSH) are open in firewalls that may be present.

⚠ CAUTION: Users may need administrative privileges on their computers to install the Agendia Service Connector and/or to configure firewalls. Consult your IT Department for assistance.

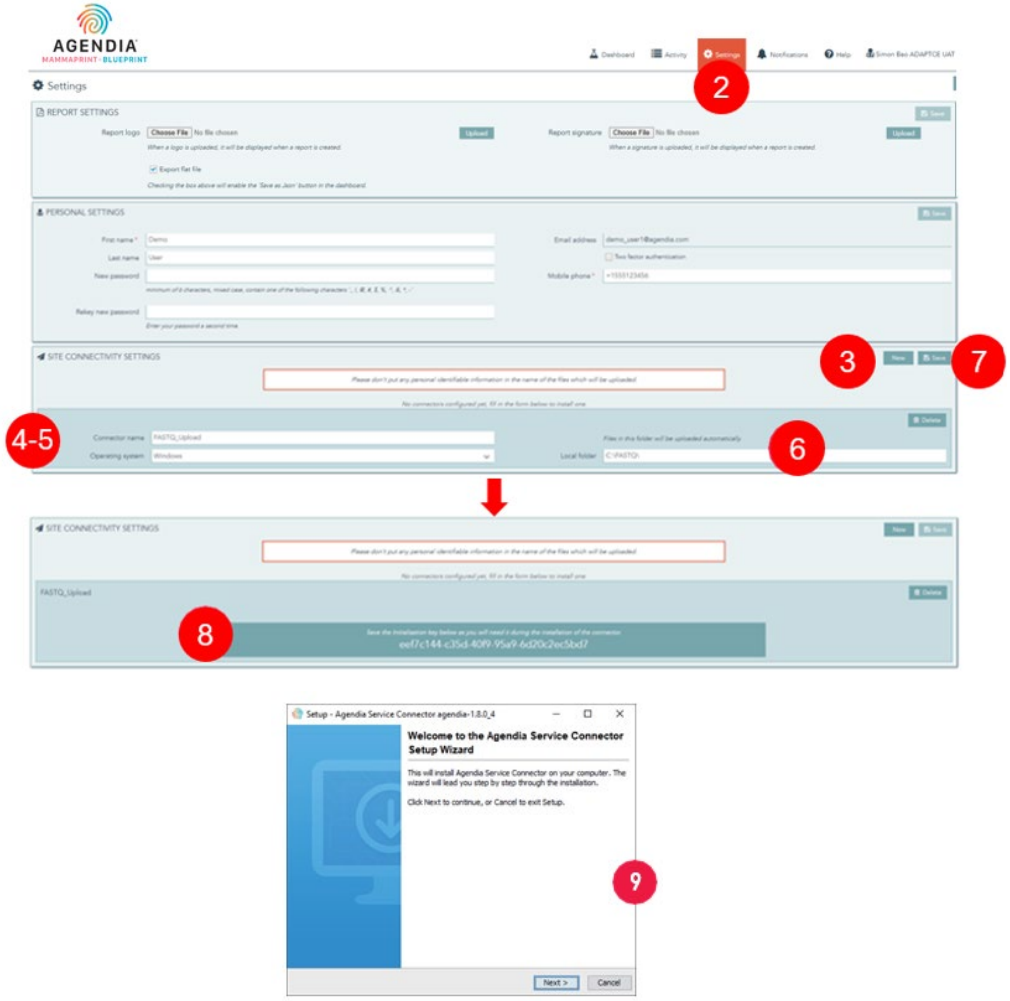




Initial Setup

CREATING AN ADAPT-CE ACCOUNT

1. An automated registration email is sent from Illumina ICA which provides a link to the ADAPT-CE registration portal.
2. Open the link in the email to go to the ADAPT-CE registration portal.
3. Enter the requested information,
   a. First Name & Last Name for your account
   b. To adhere to security requirements, the chosen password must include at least one of the following characters: ! . @ # $ % ^ & * -
4. Review Terms and Conditions and click the check box to Accept.
5. Once you click on "Register", ADAPT-CE will have registered your account details.
6. The page will now refresh with the login screen. Enter your credentials to access your newly registered account.



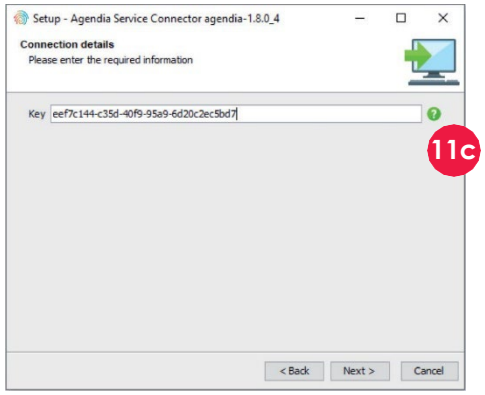
INSTALLING THE AGENDIA SERVICE CONNECTOR

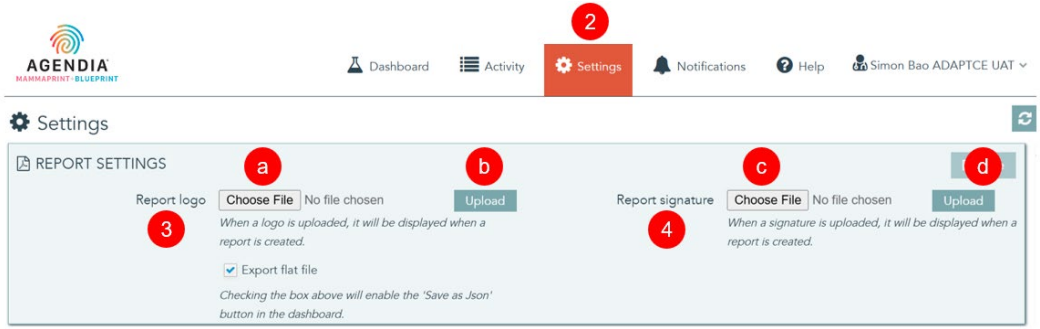
To upload data to ADAPT-CE, you will need to download and install the Agendia Service Connector to ensure a secure and robust file transfer protocol.

⚠ CAUTION: Please consult with your IT Department before installing any software in your business environment.

In addition, the ADAPT-CE connector requires the installation and operation of the program to be on a **local drive**.

1. Log into ADAPT-CE at https://ica.illumina.com/ADAPT-CE.
   When logging in some browsers, users may need to click "Sign In" twice.
2. In the ADAPT-CE top menu bar, click on "Settings".
3. In the section titled "Site Connectivity Settings", click "New".
4. Enter a unique name for your connector. e.g., "[Site Name] ADAPT-CE Connector".
5. Select your Operating System from the drop-down list (Windows, Mac or Linux).
   a. If you do not know your computer's Operating System, consult with your IT department for assistance.
6. For the "Local folder", provide the Local directory path for the folder containing the relevant FASTQ files that need to be uploaded to ADAPT-CE for analysis.
   a. Example: "C:\ADAPT_Connector\FASTQ Uploads"
7. Click "Save" to record the settings.
8. ADAPT-CE will now display an initialization key vital to the installation. Please copy/paste this key to a safe and retrievable location as you will need the key in the next installation step.
9. ADAPT-CE will then open a dialog box allowing you to save the installer for the Agendia Service Connector.
10. Select a **local drive** location on your computer and save the Agendia Service Connector installer.

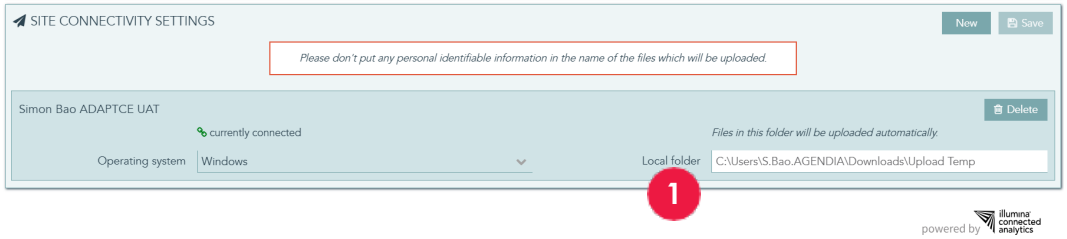




11. Once the Service Connector Installer is downloaded, navigate to the location of the saved program and initialize the Installer.
    a. Follow the instructions in the installer and click "Next" as prompted.
    b. Select the local drive installation directory.
    c. Enter or paste the initialization key that was provided by ADAPT-CE from Step 8.
    d. Installation will now initiate.
    e. When installation is complete, click "Finish" to exit the Installer.
    f. Upon successful installation, a "currently connected" status will appear in the "Site Connectivity Settings".
    g. The Agendia Service Connector is now ready for use.

CUSTOMIZING ADAPT-CE REPORTS [OPTIONAL]

1. Log into ADAPT-CE at https://ica.illumina.com/ADAPT-CE.
2. Click "Settings" in the top menu bar and navigate to "Report Settings".
3. To add a logo, go to "Report Logo".
    a. Click "Choose File" and navigate to the logo file location. Logo file format must be one of the following: JPEG, GIF, BMP, or PNG and cannot be larger than 5 megabytes (MB).
    b. Once chosen, click "Upload". A preview of logo will now display.
    Note: Logo will be affixed to the upper right corner of both the "Technical Report" and "Explanation of Results".
4. To add a signature, go to "Report Signature".
    c. Click "Choose File" and navigate to the location of your signature file. Signature file format must be one of the following: JPEG, GIF, BMP, or PNG and cannot be larger than 5 megabytes (MB).
    d. Once chosen, click "Upload". A preview of the signature will now display.
    Note: Signature will appear in the lower left section of the "Technical Report" in the "Authorized Signature" box.
5. To reset uploaded graphics, click on the respective logo/signature trash button.
6. A check marked "Export flat file" allows users to download .json files for further customization of reports.



Using ADAPT-CE

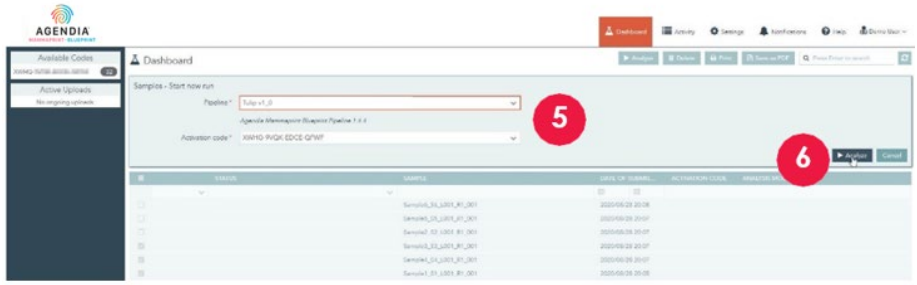
UPLOADING FASTQ FILES

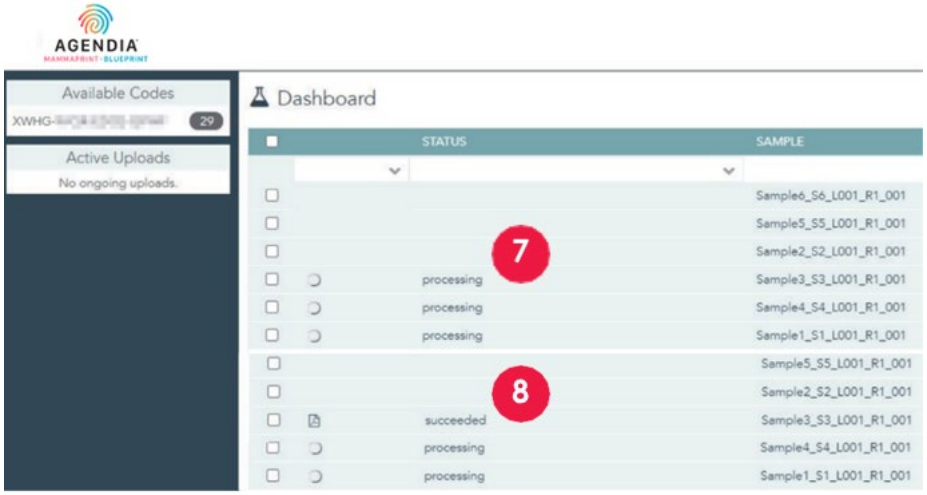
⚠ CAUTION: To ensure the privacy of your patients, do not include any personally identifiable information (PII) in the file names of your FASTQ files.

⚠ CAUTION: The file names must only contain alphanumeric characters (0-9, a-z, A-Z), and underscore characters (_). File extension must be in lowercased ".fastq.gz" format. E.g., "ABC_123.fastq.gz"

⚠ CAUTION: DO NOT alter the contents of your FASTQ files. Doing so may cause incorrect results to be generated or may prevent ADAPT-CE from processing.

1. When ready for uploading, copy the FASTQ file(s) into the directory specified during step 6 of "Installing the Agendia Service Connector".
   a. If you do not see file extensions in your file browser, please contact your IT Department for assistance.
2. The Agendia Service Connector will detect when new FASTQ files are present and will automatically upload them to ADAPT-CE.
3. Log into ADAPT-CE at https://ica.illumina.com/ADAPT-CE.
4. Ongoing uploads are shown in the "Active Uploads" section in ADAPT-CE.
5. Upon a successful upload, the FASTQ file will appear on the Dashboard.
6. FASTQ files can now be analyzed to generate reports.



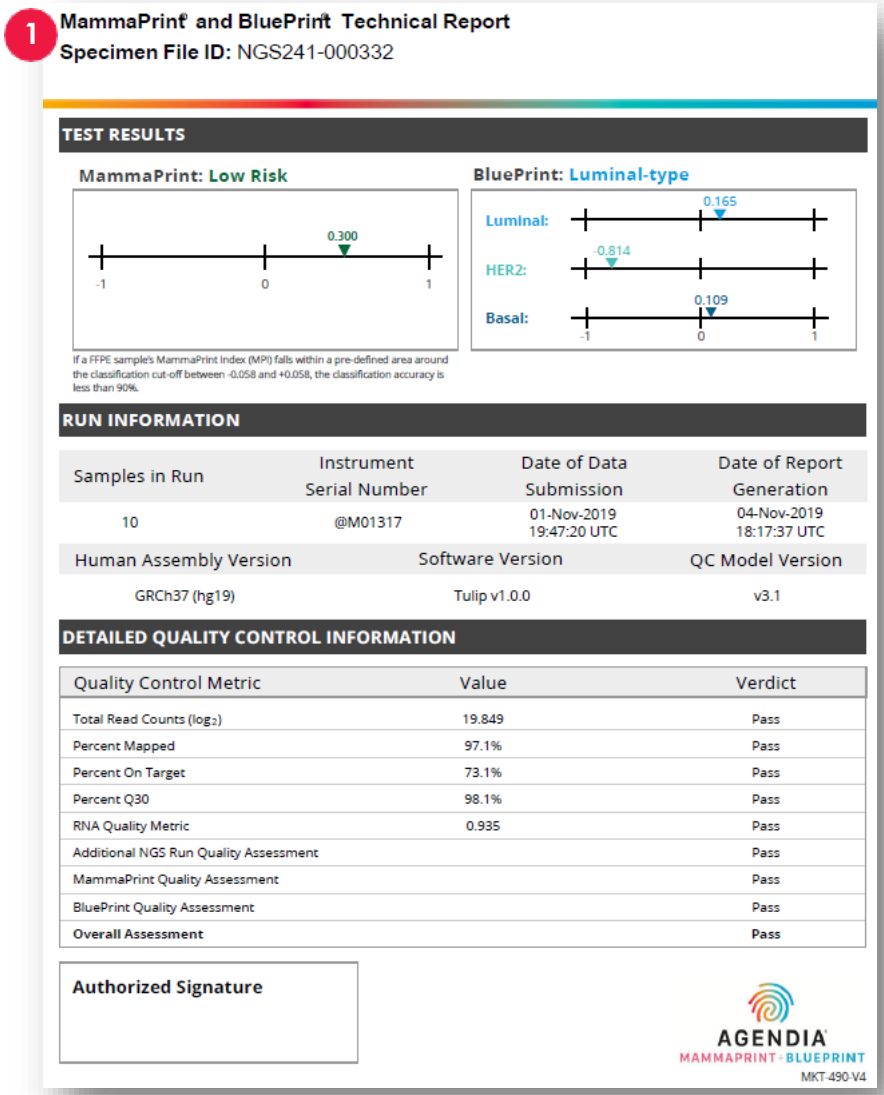


ANALYZING DATA

1. Log into ADAPT-CE at https://ica.illumina.com/ADAPT-CE.
2. Click "Dashboard" in the top menu bar.
3. Select the FASTQ file(s) you want to analyze by clicking the respective check boxes on the same row as the sample.
4. Click "Analyze".
5. You will be prompted to enter the "Pipeline" and "Activation code" to set up the analysis settings.
   ⚠ CAUTION: Make sure that the Available Codes you select has sufficient remaining reactions for your planned analysis. If you have insufficient reactions for your planned analysis, you will need to split your batch to conform with remaining kit codes.
6. Once you have confirmed the entries, click "Analyze" to start the analysis of the FASTQ file(s).
7. During data analysis, the status field next to the relevant FASTQ file(s) will show as "processing".
8. Upon completion of data analysis, the status field next to the relevant FASTQ file(s) will change to "succeeded".

DOWNLOADING REPORTS

1. Log into ADAPT-CE at https://ica.illumina.com/ADAPT-CE.
2. Click on "Dashboard" in the top menu bar.
3. To print reports:
   a. Click the check box next to the file(s) and click "Print".
   b. Your PDF reader software will open the selected file(s).
   c. The Technical Report and Explanation of Results reports can now be printed.
4. To save reports:
   a. Click the check box next to the file(s) and click "Save as PDF".
   b. Your PDF reader software will open the selected file(s).
   c. Save the reports to a directory of your choice.
   Note: According to system data retention policies, PDF reports are deleted after one year, while FASTQ files are removed after 30 days.



1

MammaPrint® and BluePrint® Technical Report
Specimen File ID: NGS241-000332

TEST RESULTS

MammaPrint: Low Risk

BluePrint: Luminal-type

If a FFPE sample's MammaPrint Index (MPI) falls within a pre-defined area around the classification cut-off between -0.058 and +0.058, the classification accuracy is less than 90%.

RUN INFORMATION

Samples in Run	Instrument Serial Number	Date of Data Submission	Date of Report Generation
10	@M01317	01-Nov-2019 19:47:20 UTC	04-Nov-2019 18:17:37 UTC

Human Assembly Version	Software Version	QC Model Version
GRCh37 (hg19)	Tulip v1.0.0	v3.1

DETAILED QUALITY CONTROL INFORMATION

Quality Control Metric	Value	Verdict
Total Read Counts (log_2)	19.849	Pass
Percent Mapped	97.1%	Pass
Percent On Target	73.1%	Pass
Percent Q30	98.1%	Pass
RNA Quality Metric	0.935	Pass
Additional NGS Run Quality Assessment		Pass
MammaPrint Quality Assessment		Pass
BluePrint Quality Assessment		Pass
Overall Assessment		**Pass**

Authorized Signature

AGENDIA
MAMMAPRINT + BLUEPRINT
MKT-490-V4

ADAPT-CE Reports

ADAPT-CE generates two reports, the "Technical Report" and the "Explanation of Results". In this User Guide, an example case with a Low Risk MammaPrint result and a Luminal A BluePrint result will be used to illustrate the utility of the Technical Report and Explanation of Results. The two reports are combined in a single PDF.

A. TECHNICAL REPORT (TR)

The TR is provided as a tool to provide a high-level overview of the test results, run information and related quality control information.

B. EXPLANATION OF RESULTS (EOR)

The EoR is provided as a tool to supplement the results provided in the TR described above. The Explanation of Results explains the MammaPrint and BluePrint results in the context of published clinical data.

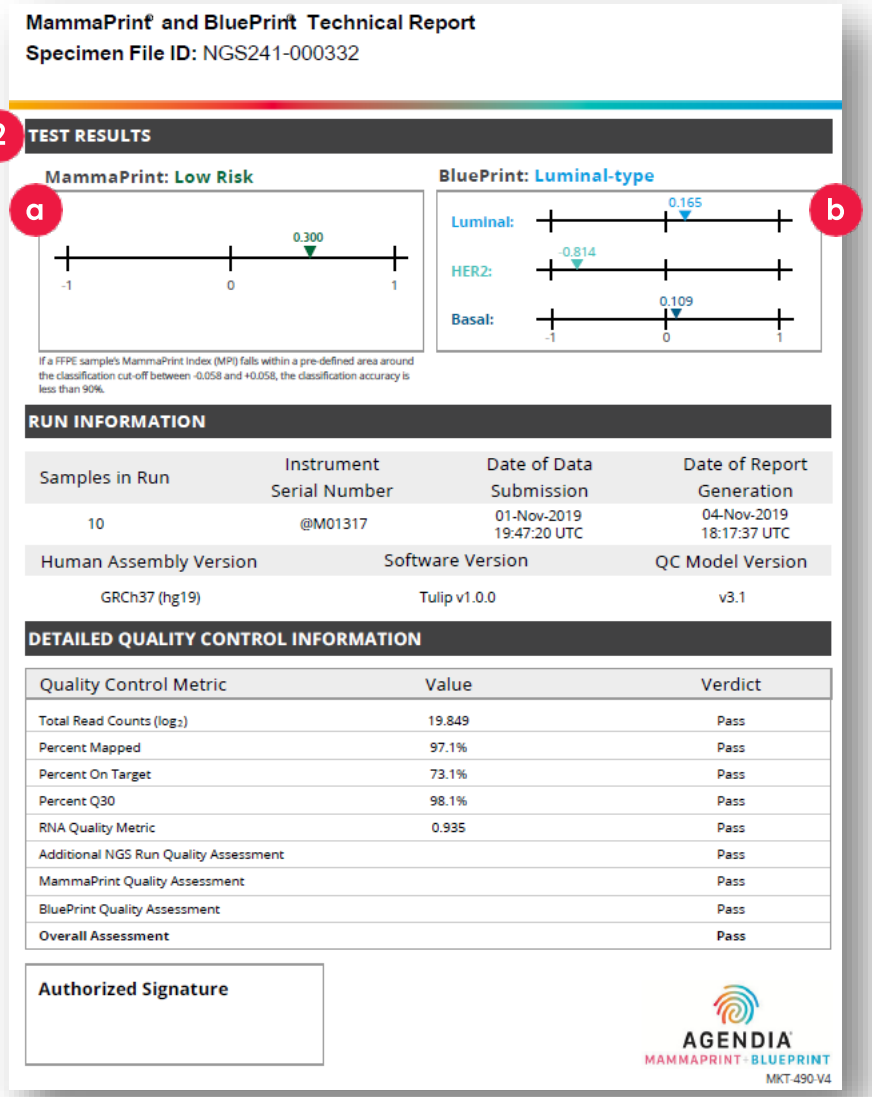
Technical Report

The Technical Report contains the following sections:

1. **Specimen File ID**
2. **TEST RESULTS**
   a. MammaPrint
   b. BluePrint
3. **RUN INFORMATION**
4. **DETAILED QUALITY CONTROL INFORMATION**

1. SPECIMEN FILE ID

⚠ CAUTION: Users are responsible for ensuring that all uploaded files are de-identified. The Specimen File ID is the name of the FASTQ file that was analyzed to generate the Technical Report. To ensure the privacy of your patients, DO NOT include any personally identifiable information (PII) in your FASTQ file name. ADAPT-CE will not match the Specimen File ID to any other information.



MammaPrint® and BluePrint® Technical Report

Specimen File ID: NGS241-000332

2 **TEST RESULTS**

MammaPrint: Low Risk (a)

BluePrint: Luminal-type (b)

If a FFPE sample's MammaPrint Index (MPI) falls within a pre-defined area around the classification cut-off between -0.058 and +0.058, the classification accuracy is less than 90%.

RUN INFORMATION

Samples in Run	Instrument Serial Number	Date of Data Submission	Date of Report Generation
10	@M01317	01-Nov-2019 19:47:20 UTC	04-Nov-2019 18:17:37 UTC
Human Assembly Version	**Software Version**		**QC Model Version**
GRCh37 (hg19)	Tulip v1.0.0		v3.1

DETAILED QUALITY CONTROL INFORMATION

Quality Control Metric	Value	Verdict
Total Read Counts (log_2)	19.849	Pass
Percent Mapped	97.1%	Pass
Percent On Target	73.1%	Pass
Percent Q30	98.1%	Pass
RNA Quality Metric	0.935	Pass
Additional NGS Run Quality Assessment		Pass
MammaPrint Quality Assessment		Pass
BluePrint Quality Assessment		Pass
Overall Assessment		**Pass**

Authorized Signature

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MKT-490-V4

2. TEST RESULTS

a. MAMMAPRINT TEST RESULT

The MammaPrint result is provided as a binary result of either "Low Risk" or "High Risk" for risk of recurrence. The prognostic profile (Low Risk, High Risk) of the sample is determined by calculating the MammaPrint Index (MPI) on a scale of -1.000 to +1.000

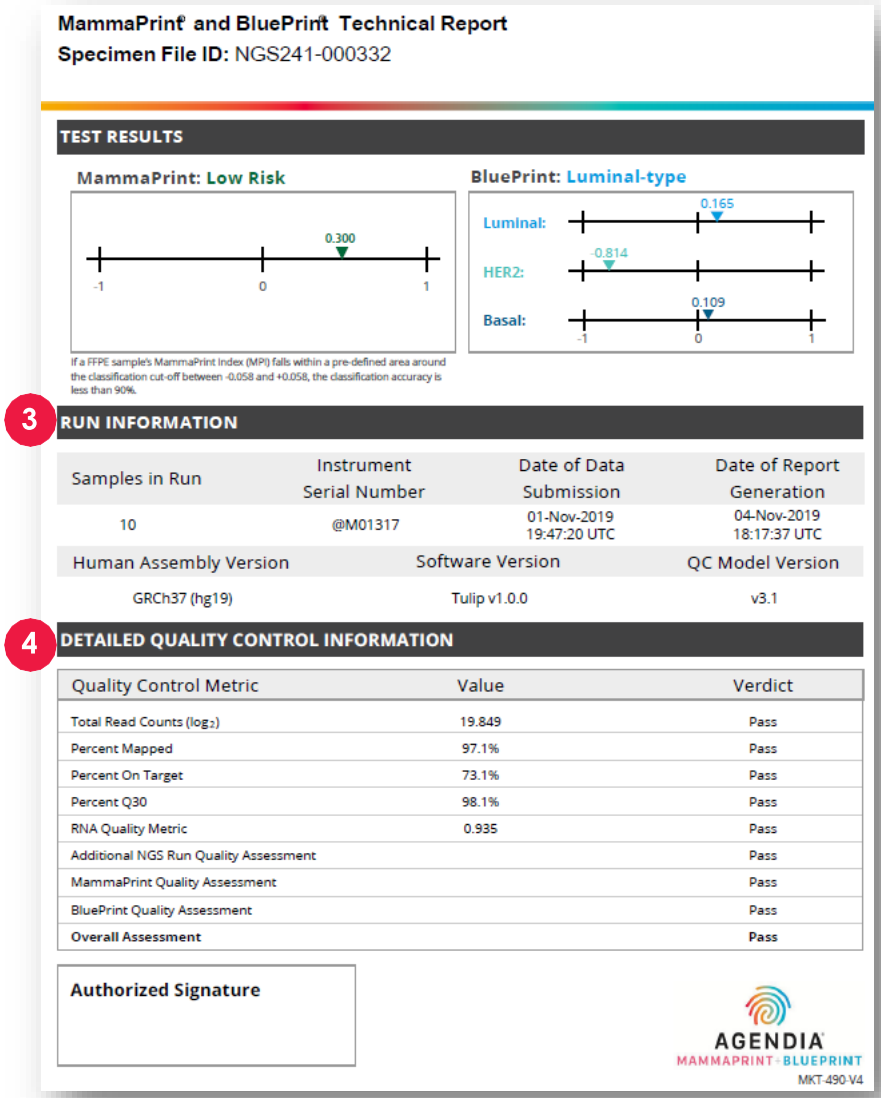
- High Risk results are those that are equal to or below 0.000
- Low Risk results are those that are above 0.000

If the MammaPrint Index (MPI) falls within a pre-defined area around the classification cut-off between -0.058 and +0.058, the classification accuracy is less than 90%.

Note: EoR will further elaborate on various MammaPrint Risk Groups.

b. BLUEPRINT TEST RESULT

The BluePrint result is provided as Luminal-type, HER2-type, or Basal-type. The subtype with the highest value is the dominant subtype and hence is the outcome of BluePrint. In the case of subtypes having the same index value, the result will display: "Mixed-subtype".



MammaPrint® and BluePrint® Technical Report
Specimen File ID: NGS241-000332

TEST RESULTS

MammaPrint: Low Risk

BluePrint: Luminal-type

If a FFPE sample's MammaPrint Index (MPI) falls within a pre-defined area around the classification cut-off between -0.058 and +0.058, the classification accuracy is less than 90%.

3 **RUN INFORMATION**

Samples in Run	Instrument Serial Number	Date of Data Submission	Date of Report Generation
10	@M01317	01-Nov-2019 19:47:20 UTC	04-Nov-2019 18:17:37 UTC

Human Assembly Version	Software Version	QC Model Version
GRCh37 (hg19)	Tulip v1.0.0	v3.1

4 **DETAILED QUALITY CONTROL INFORMATION**

Quality Control Metric	Value	Verdict
Total Read Counts (log_2)	19.849	Pass
Percent Mapped	97.1%	Pass
Percent On Target	73.1%	Pass
Percent Q30	98.1%	Pass
RNA Quality Metric	0.935	Pass
Additional NGS Run Quality Assessment		Pass
MammaPrint Quality Assessment		Pass
BluePrint Quality Assessment		Pass
Overall Assessment		**Pass**

Authorized Signature

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MKT-490-V4

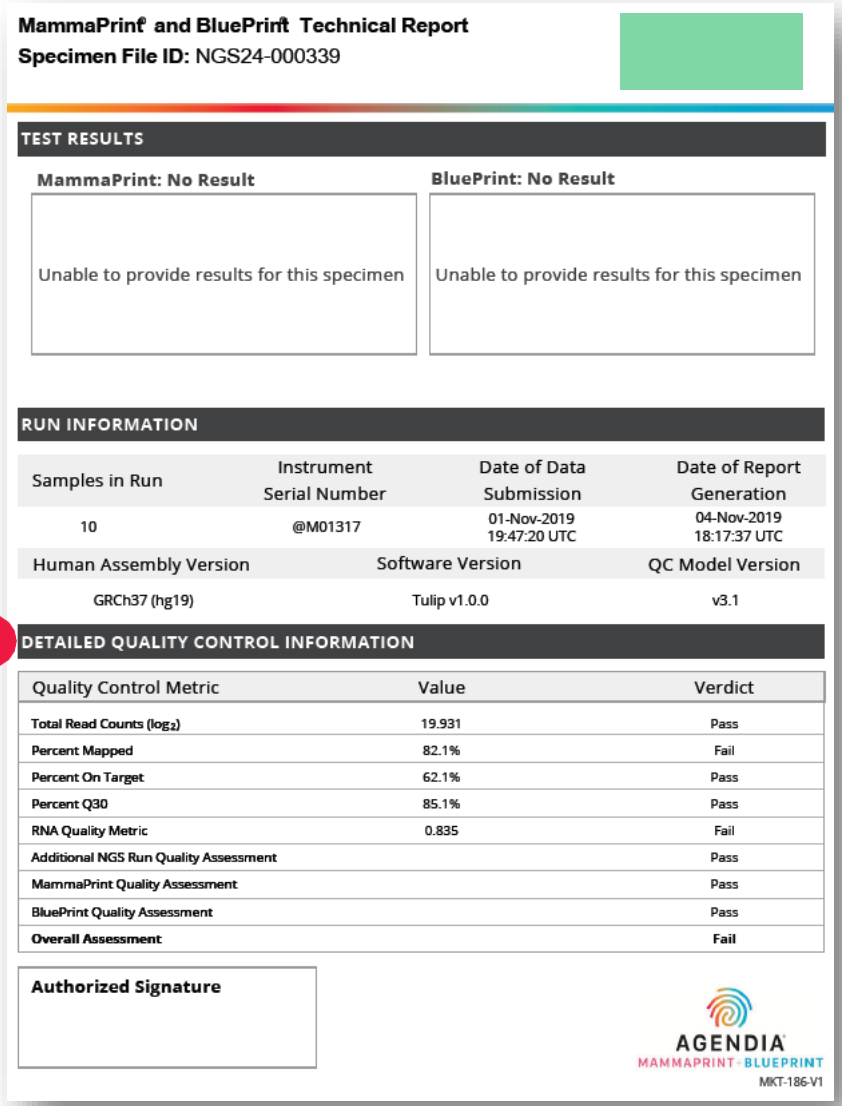
3. RUN INFORMATION

This section contains information about the analysis performed by ADAPT-CE. The table below provides additional details:

Run Information	Details
Samples in Run	The number of samples in an analysis run
Instrument Serial Number	The serial number of the MiSeq instrument
Date of Data Submission	Date FASTQs are detected and uploaded
Date of Report Generation	Date the reports are analyzed
Human Assembly Version	The version of the human genome used to map the NGS reads.
Software Version	The version of the analysis component of ADAPT-CE
QC Model Version	The version of the QC model

4. DETAILED QUALITY CONTROL INFORMATION

- This section contains various quality control (QC) metrics within an individual sample's analysis results. The Total Read Counts, Percent Mapped, Percent On Target and Percent Q30 are commonly used in analysis of RNA sequencing data.
- The RNA Quality Metric is utilized to provide insight into the overall quality of the isolated RNA.
- The other additional QC metrics are proprietary to Agendia and are part of the algorithm component of ADAPT-CE.



MammaPrint® and BluePrint® Technical Report
Specimen File ID: NGS24-000339

TEST RESULTS

MammaPrint: No Result	BluePrint: No Result
Unable to provide results for this specimen	Unable to provide results for this specimen

RUN INFORMATION

Samples in Run	Instrument Serial Number	Date of Data Submission	Date of Report Generation
10	@M01317	01-Nov-2019 19:47:20 UTC	04-Nov-2019 18:17:37 UTC
Human Assembly Version	**Software Version**		**QC Model Version**
GRCh37 (hg19)	Tulip v1.0.0		v3.1

4 **DETAILED QUALITY CONTROL INFORMATION**

Quality Control Metric	Value	Verdict
Total Read Counts (log_2)	19.931	Pass
Percent Mapped	82.1%	Fail
Percent On Target	62.1%	Pass
Percent Q30	85.1%	Pass
RNA Quality Metric	0.835	Fail
Additional NGS Run Quality Assessment		Pass
MammaPrint Quality Assessment		Pass
BluePrint Quality Assessment		Pass
Overall Assessment		**Fail**

Authorized Signature

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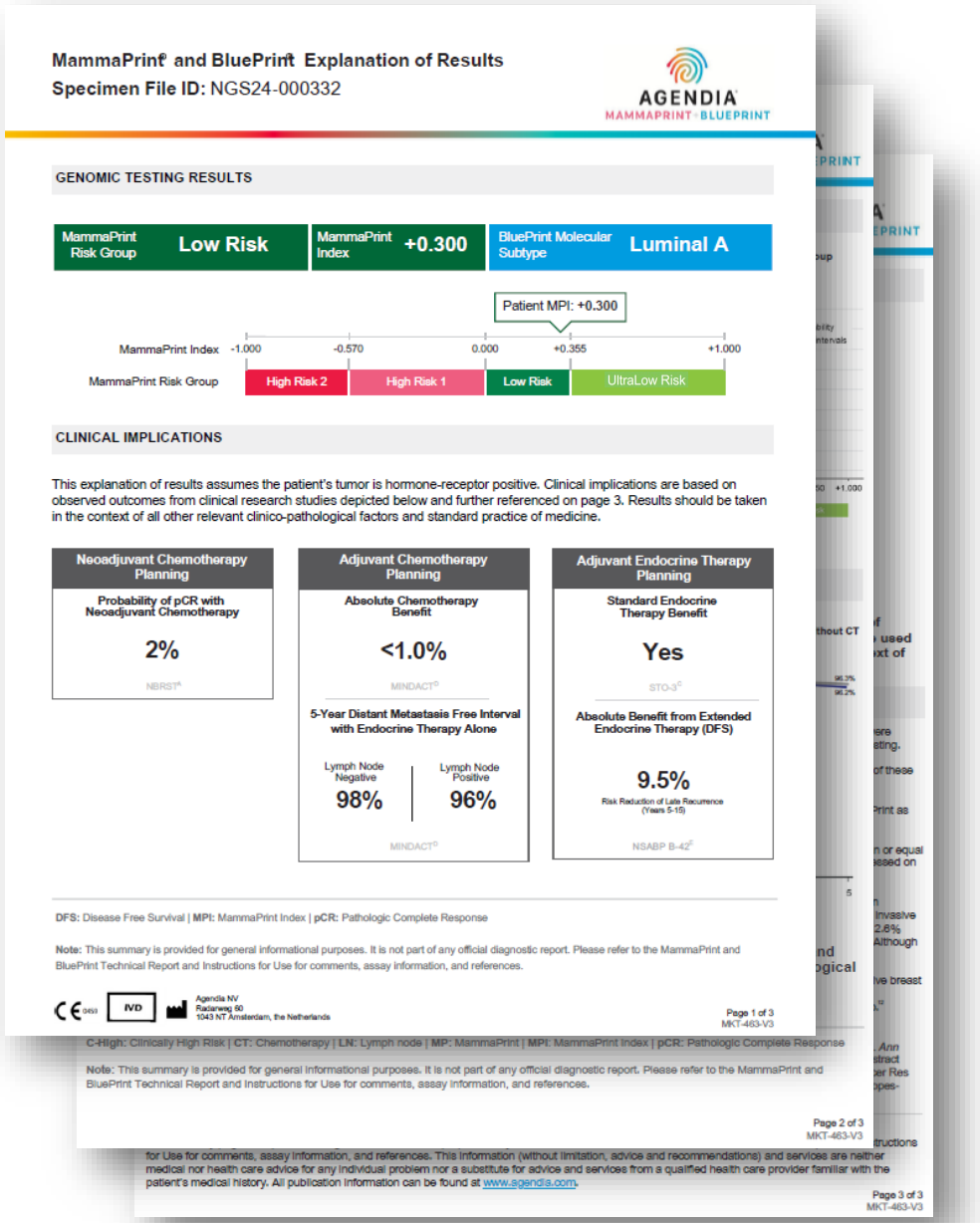
MKT-186-V1

4. DETAILED QUALITY CONTROL INFORMATION (Continued)

If any of the previously mentioned QC metrics, or a combination of QC metrics has a failure,

- Test Results section will display:
  - MammaPrint: **No Result**
  - BluePrint: **No Result**
- Run Information is static.
- Detailed Quality Control Information's Overall Assessment will display a "Fail" verdict.
- Subsequent Explanation of Results will not be provided.

Note: If a custom logo was uploaded in "CUSTOMIZING ADAPT-CE REPORTS", it will appear in the green box.



Explanation of Results (EoR)

The EoR three-page document may contain the following key sections:

EoR Summary Page (pg. 1 of 3)

1. Specimen File ID
2. Genomic Testing Results
3. Clinical Implications
   a. Neoadjuvant Chemotherapy Planning
   b. Adjuvant Chemotherapy Planning
   c. Adjuvant Endocrine Therapy Planning

EoR Chemotherapy Data (pg. 2 of 3)

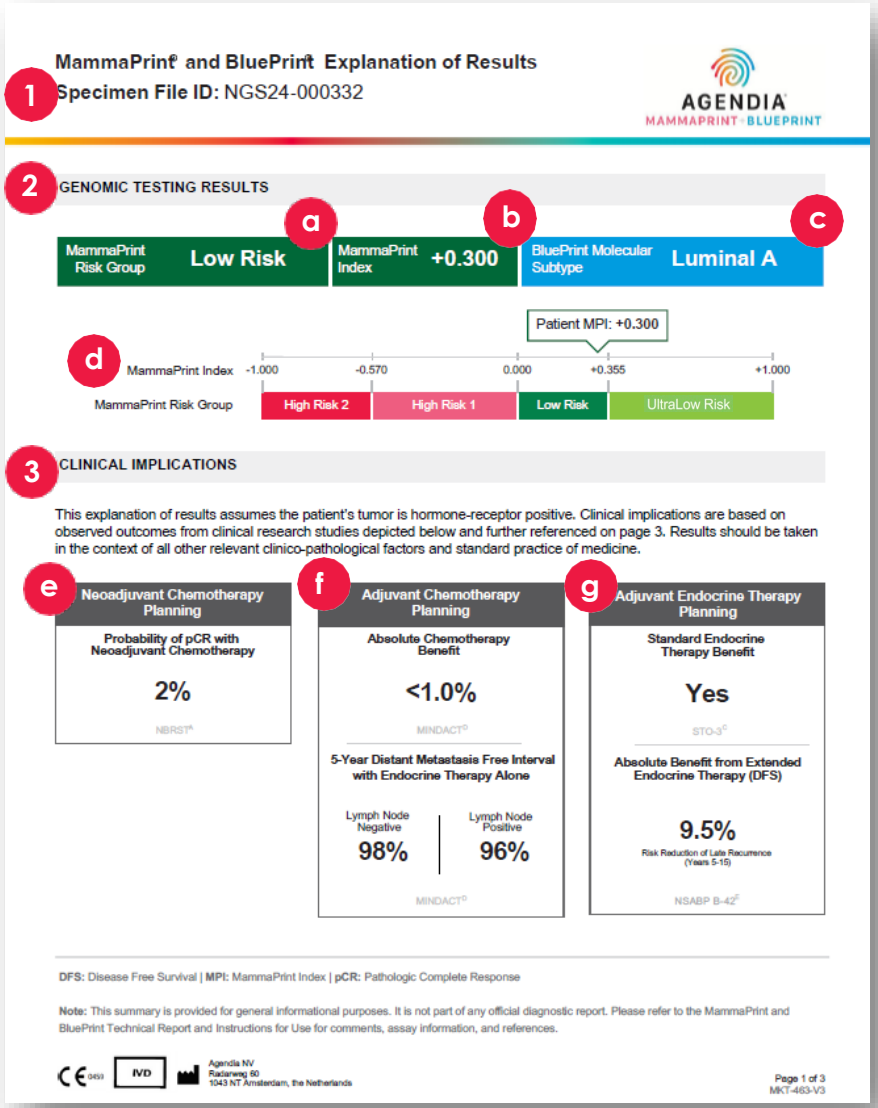
4. Neoadjuvant Chemotherapy Planning Data
5. Adjuvant Chemotherapy Planning Data

EoR Endocrine Data / References (pg. 3 of 3)

6. Adjuvant Endocrine Therapy (ET) Planning Data
7. Clinical Study and Trial References

Note:

- All 3 pages of the EoR are dynamic based on the MammaPrint and BluePrint outcomes.
- If you have uploaded a custom logo in the "CUSTOMIZING ADAPT-CE REPORTS", it will replace the Agendia logo in the top right corner of all 3 pages of the EoR.



EoR Summary Page (pg.1 of 3)

1. SPECIMEN FILE ID

⚠ CAUTION: Users are responsible for ensuring that all uploaded files are de-identified. The Specimen File ID is the name of the FASTQ file that was analyzed to generate the Technical Report. To ensure the privacy of your patients, DO NOT include any personally identifiable information (PII) in your FASTQ file name. ADAPT-CE will not match the Specimen File ID to any other information.

2. GENOMIC TESTING RESULTS

This section elaborates on the MammaPrint and BluePrint results from the Technical Report:

- **a.** MammaPrint Risk Group:
  High Risk I, High Risk 2, Low Risk and UltraLow Risk
- **b.** MammaPrint Index (4 sig figs): **+/- 1.000**
- **c.** BluePrint Molecular Subtype:
  Luminal A, Luminal B, HER2, Basal or Mixed
- **d.** MammaPrint Index plot to relative Risk Group

3. CLINICAL IMPLICATIONS

This section presents dynamic clinical information derived from the MammaPrint Risk Group and BluePrint Subtype, based on multiple clinical studies (refer to the Explanation of Results on page 3).

e. NEOADJUVANT CHEMOTHERAPY PLANNING

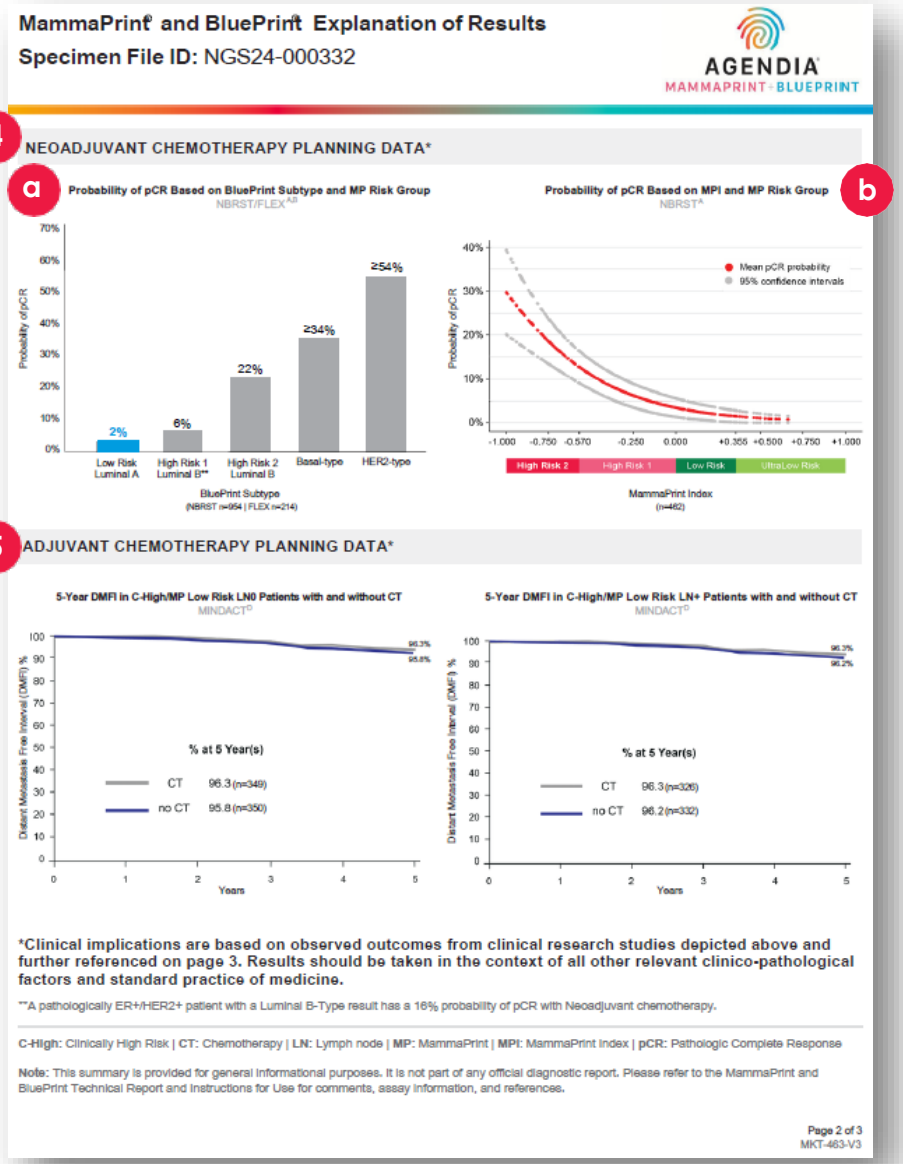
Pathological Complete Response (pCR) is determined by the BluePrint subtype unless the subtype is mixed, in which case it is based on the average pCR observed in the MammaPrint risk group.

f. ADJUVANT CHEMOTHERAPY PLANNING

Dynamic and based off MammaPrint Risk Group

g. ENDOCRINE THERAPY PLANNING

Dynamic and based off MammaPrint Risk Group



EoR Chemotherapy Data (pg. 2 of 3)

4. NEOADJUVANT CHEMOTHERAPY PLANNING DATA

a. Probability of pCR Based on BluePrint Subtype and MP Risk group. See NBRST/FLEX[A, B] on page 3 of EoR for additional details. Respective result will be highlighted with the probability of pCR.

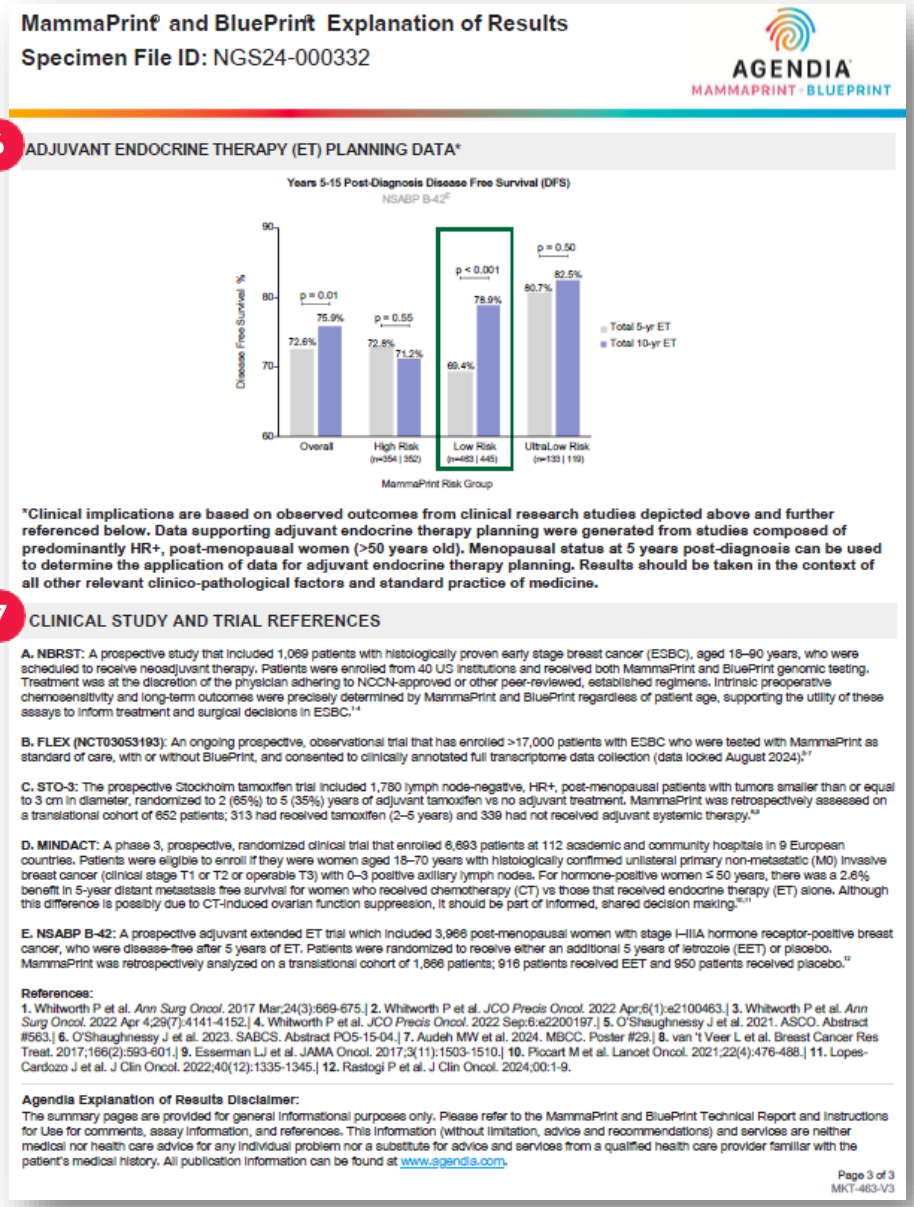
- Low Risk Luminal A: 2%
- High Risk 1 Luminal B: 6%
- High Risk 2 Luminal B: 22%
- Basal type: ≥34%
- HER2-type: ≥54%
- Mixed Subtype: no highlight

b. Probability of pCR Based on MammaPrint Index and MammaPrint Risk Group. See NBRST[A] on page 3 of EoR for additional details.

5. ADJUVANT CHEMOTHERAPY PLANNING DATA

Dynamic and based off MammaPrint Risk Group

- UltraLow Risk will illustrate 8-year outcomes
- All other risk groups have 5-year outcomes
- Depending on results see Page 3 for respective studies
  UltraLow Risk and Low Risk – See MINDACT[D]
  High Risk 1 & High Risk 2 – See FLEX/Knauer[B/F]



MammaPrint® and BluePrint Explanation of Results

Specimen File ID: NGS24-000332

AGENDIA MAMMAPRINT + BLUEPRINT

6 ADJUVANT ENDOCRINE THERAPY (ET) PLANNING DATA*

Years 5-15 Post-Diagnosis Disease Free Survival (DFS)

NSABP B-42[F]

***Clinical implications are based on observed outcomes from clinical research studies depicted above and further referenced below. Data supporting adjuvant endocrine therapy planning were generated from studies composed of predominantly HR+, post-menopausal women (>50 years old). Menopausal status at 5 years post-diagnosis can be used to determine the application of data for adjuvant endocrine therapy planning. Results should be taken in the context of all other relevant clinico-pathological factors and standard practice of medicine.**

7 CLINICAL STUDY AND TRIAL REFERENCES

A. NBRST: A prospective study that included 1,069 patients with histologically proven early stage breast cancer (ESBC), aged 18–90 years, who were scheduled to receive neoadjuvant therapy. Patients were enrolled from 40 US institutions and received both MammaPrint and BluePrint genomic testing. Treatment was at the discretion of the physician adhering to NCCN-approved or other peer-reviewed, established regimens. Intrinsic preoperative chemosensitivity and long-term outcomes were precisely determined by MammaPrint and BluePrint regardless of patient age, supporting the utility of these assays to inform treatment and surgical decisions in ESBC.[1-4]

B. FLEX (NCT03053193): An ongoing prospective, observational trial that has enrolled >17,000 patients with ESBC who were tested with MammaPrint as standard of care, with or without BluePrint, and consented to clinically annotated full transcriptome data collection (data locked August 2024).[5-7]

C. STO-3: The prospective Stockholm tamoxifen trial included 1,780 lymph node-negative, HR+, post-menopausal patients with tumors smaller than or equal to 3 cm in diameter, randomized to 2 (65%) to 5 (35%) years of adjuvant tamoxifen vs no adjuvant treatment. MammaPrint was retrospectively assessed on a translational cohort of 652 patients; 313 had received tamoxifen (2–5 years) and 339 had not received adjuvant systemic therapy.[8,9]

D. MINDACT: A phase 3, prospective, randomized clinical trial that enrolled 6,693 patients at 112 academic and community hospitals in 9 European countries. Patients were eligible to enroll if they were women aged 18–70 years with histologically confirmed unilateral primary non-metastatic (M0) invasive breast cancer (clinical stage T1 or T2 or operable T3) with 0–3 positive axillary lymph nodes. For hormone-positive women ≤ 50 years, there was a 2.6% benefit in 5-year distant metastasis free survival for women who received chemotherapy (CT) vs those that received endocrine therapy (ET) alone. Although this difference is possibly due to CT-induced ovarian function suppression, it should be part of informed, shared decision making.[10,11]

E. NSABP B-42: A prospective adjuvant extended ET trial which included 3,966 post-menopausal women with stage I–IIIA hormone receptor-positive breast cancer, who were disease-free after 5 years of ET. Patients were randomized to receive either an additional 5 years of letrozole (EET) or placebo. MammaPrint was retrospectively analyzed on a translational cohort of 1,866 patients; 916 patients received EET and 950 patients received placebo.[12]

References:

1. Whitworth P et al. *Ann Surg Oncol*. 2017 Mar;24(3):669-675.| **2.** Whitworth P et al. *JCO Precis Oncol*. 2022 Apr;6(1):e2100463.| **3.** Whitworth P et al. *Ann Surg Oncol*. 2022 Apr 4;29(7):4141-4152.| **4.** Whitworth P et al. *JCO Precis Oncol*. 2022 Sep:6:e2200197.| **5.** O'Shaughnessy J et al. 2021. ASCO. Abstract #563.| **6.** O'Shaughnessy J et al. 2023. SABCS. Abstract PO5-15-04.| **7.** Audeh MW et al. 2024. MBCC. Poster #29.| **8.** van 't Veer L et al. Breast Cancer Res Treat. 2017;166(2):593-601.| **9.** Esserman LJ et al. JAMA Oncol. 2017;3(11):1503-1510.| **10.** Piccart M et al. Lancet Oncol. 2021;22(4):476-488.| **11.** Lopes-Cardozo J et al. J Clin Oncol. 2022;40(12):1335-1345.| **12.** Rastogi P et al. J Clin Oncol. 2024;00:1-9.

Agendia Explanation of Results Disclaimer:
The summary pages are provided for general informational purposes only. Please refer to the MammaPrint and BluePrint Technical Report and Instructions for Use for comments, assay information, and references. This information (without limitation, advice and recommendations) and services are neither medical nor health care advice for any individual problem nor a substitute for advice and services from a qualified health care provider familiar with the patient's medical history. All publication information can be found at www.agendia.com.

EoR Endocrine Data / References (pg. 3 of 3)

6. Adjuvant Endocrine Therapy (ET) Planning Data

Dynamic and based off MammaPrint Risk Group

- UltraLow has additional STO-3[C]
- Risk groups will be boxed per NSABP B-42[E]

7. Clinical Study and Trail References

A. NBRST
B. FLEX (NCT03053193)
C. STO-3
D. MINDACT
E. NSABP B-42
F. Knauer (added for High Risk 1 or High Risk 2)

References:

1. Whitworth P et al. *Ann Surg Oncol*. 2017 Mar;24(3):669-675.
2. Whitworth P et al. *JCO Precis Oncol*. 2022 Apr;6(1):e2100463.
3. Whitworth P et al. *AnnSurg Oncol*. 2022 Apr 4;29(7):4141-4152.
4. Whitworth P et al. *JCO Precis Oncol*. 2022 Sep:6:e2200197.
5. O'Shaughnessy J et al. 2021. ASCO. Abstract#563.
6. O'Shaughnessy J et al. 2023. SABCS. Abstract PO5-15-04.
7. Audeh MW et al. 2024. MBCC. Poster #29.
8. van 't Veer L et al. Breast Cancer ResTreat. 2017;166(2):593-601.
9. Esserman LJ et al. JAMA Oncol. 2017;3(11):1503-1510.
10. Piccart M et al. Lancet Oncol. 2021;22(4):476-488.
11. Lopes-Cardozo J et al. J Clin Oncol. 2022;40(12):1335-1345.
12. Rastogi P et al. J Clin Oncol. 2024;00:1-9.

Note: The following two References are inserted for High Risk 1/II

- Brufsky A et al. 2024. SABCS. P2-08-12
- Knauer M et al. Breast Cancer Res Treat. 2010;120(3):655-61.

Troubleshooting

- The following Troubleshooting points pertain to topics related to ADAPT-CE setup and operation.
- For an additional list of troubleshooting topics, please refer to the Help tab at the top right of the ADAPT-CE interface.

Problem	Solution
Forgot your password to ADAPT-CE.	Go to the login screen from https://ica.illumina.com/ADAPT-CE. Click on the "Forgot password?" link and follow the instructions provided. If you still are unable to login, contact NGS.support@agendia.com for additional assistance.
Experiencing issues with setting up the Agendia Service Connector.	Go to the "Settings" section of ADAPT-CE and click "Delete" on the connector you are having issues with. Ensure a local folder on the computer is established and follow steps to install another uniquely named connector.
Files are not being uploaded to ADAPT-CE via the Agendia Service Connector.	Go to the "Settings" section of ADAPT-CE and ensure that the "Local folder" listed for the Agendia Service Connector matches the directory where the FASTQ files are.
Pages in ADAPT-CE are not functioning as expected.	Click the "Refresh" button on the page. If the problem persists, contact NGS.support@agendia.com.
Duplicate FASTQ files appear within ADAPT-CE.	Ensure that FASTQ files are uploaded only once when using the Agendia Secure Connector. In the event that duplicates are uploaded, navigate to the Agendia Secure Connector upload folder, delete the duplicates and reupload a single file.
The result for a sample only includes a Technical Report and does not include an Explanation of Results (EoR) document.	Check the verdict for the Overall Assessment. If it says "Fail", then no Explanation of Results (EoR) is generated for the sample.
Sample reports cannot be saved or printed.	Ensure that the status field next to the sample on the "Dashboard" page says "succeeded" and that a PDF icon is shown.
FASTQ files remain hanging underneath "Active Uploads" after deleting the FASTQ file from the connector or after successful FASTQ file upload into the Dashboard.	Click the "Abort Data Transfer Functionality" button within "Active Uploads" for the hanging FASTQ file that you wish to remove.

Miscellaneous

SECURITY

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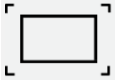
BROWSER SESSION TIMEOUT AND SYMBOLS

For security purposes, after 15 minutes of inactivity in the browser, the software will automatically end your session and sign you out. A warning message will be displayed prior to signing you out, giving you the option to stay signed in.

Symbol	Title of Symbol	Description of Symbol
	Manufacturer	Indicates the medical device manufacturer, as defined in EU Directives 90/385/EEC, 93/42/EEC and 98/79/EC.
	Caution	Indicates the need for the user to consult the instructions for use for important cautionary information such as warnings and precautions that cannot, for a variety of reasons, be presented on the medical device itself.
	In vitro diagnostic medical device	Indicates a medical device that is intended to be used as an in vitro diagnostic medical device.

If you have any questions regarding this product, please contact NGS.Support@agendia.com or by telephone at +31 (0) 20 462 1510, Monday to Friday from 08:30 to 17:00 (GMT/UTC +1).

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Agendia NV
Radarweg 60
1043 NT Amsterdam
The Netherlands

CE 0459

IVD

MAMMAPRINT+BLUEPRINT
Illuminating Tumor Biology

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