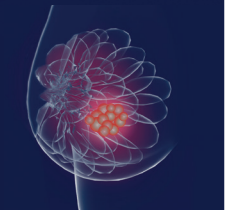


**KEY**conversations

*in early-stage TNBC. Let's keep talking*

# Optimising treatment outcomes in early-stage triple-negative breast cancer January 2023

## Highlights Report

**Adverse events should be reported.**
**Reporting forms and information can be found at www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.**
**Adverse events should also be reported to MSD, UK (Tel: 0208 1548000)**

This promotional and educational meeting was organised and fully funded by MSD.

Please click the following links for the KEYTRUDA SmPC and prescribing information: **Great Britain**; **Northern Ireland**.

Please consult the SmPC for further information before making any prescribing decision

MSD




# KEYconversations in early-stage TNBC: KEYTRUDA (pembrolizumab) Launch Meeting Highlights

The MSD KEYTRUDA Launch Meeting in early-stage triple-negative (TNBC) breast cancer took place on the 27th of January 2023 at the Hilton London Tower Bridge. The event was chaired by Professor Peter Schmid, MD PhD FRCP (Consultant Medical Oncologist, Barts Cancer Institute, London).

Throughout multiple presentations, panel discussions, workshops and Q&A sessions, panelists entered into a discussion about the evolving treatment landscape for early-stage triple-negative breast cancer. The panelists also explored the data, rationale and patient eligibility for immuno-oncology (IO) as neo-adjuvant and adjuvant treatment in early-stage TNBC, and further examined adverse event management for patients being treated with IO for early-stage TNBC. Attendees were able to participate in the discussion through interactive workshops and via a digital polling system.

# Content

**Panel Discussion:** Variation in use of neo-adjuvant therapy
*Chair: Mr Henry Cain, Consultant Oncoplastic Breast Surgeon, Royal Victoria Infirmary, Newcastle Upon Tyne.*

**Presentation:** Immunotherapy in early-stage TNBC
*Prof. Peter Schmid, Consultant Medical Oncologist, Barts Cancer Institute, London.*

**Panel Discussion:** Individualising care for early TNBC patients
*Chair: Dr Judy King, Consultant Medical Oncologist, Royal Free Hospital and Barnet Hospital, London.*

**Presentation:** Identification and management of immunotherapy related adverse events
*Dr Melissa Phillips, Consultant Medical Oncologist, Barts Cancer Institute, London.*
*Dr Fharat Raja, Consultant Medical Oncologist, University College London Hospitals NHS Foundation Trust, London and Dr Duncan Wheatley, Consultant Clinical Oncologist, Royal Cornwall Hospital NHS Trust.*

# Workshops:



**Workshop 1:** Optimising adverse event management pathways
*Dr Judy King, Consultant Medical Oncologist, Royal Free Hospital and Barnet Hospital, London.*
*Dr Melissa Phillips, Consultant Medical Oncologist, Barts Cancer Institute, London.*

**Workshop 2:** Optimising management of the axilla post neo-adjuvant treatment
*Dr Duncan Wheatley, Consultant Clinical Oncologist, Royal Cornwall Hospital NHS Trust.*
*Mr Stuart McIntosh, Consultant Breast Surgeon, Belfast City Hospital, Belfast.*

**Workshop 3:** Optimising conversations with the younger TNBC patient
*Dr Fharat Raja, Consultant Medical Oncologist, University College London Hospitals NHS Foundation Trust, London.*
*Mr Henry Cain, Consultant Oncoplastic Breast Surgeon, Royal Victoria Infirmary, Newcastle Upon Tyne.*
*Mrs Claire Phelan, Clinical Nurse Specialist, Royal Free Hospital, London.*

# Variation in use of neo-adjuvant therapy

**Chair: Mr Henry Cain** (Consultant Oncoplastic Breast Surgeon, Royal Victoria Infirmary, Newcastle Upon Tyne)

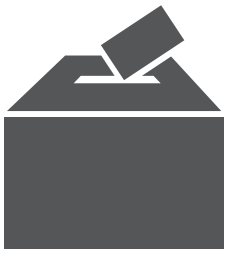
**Panel: Dr Judy King** (Consultant Medical Oncologist, Royal Free Hospital and Barnet Hospital London);
**Mr Stuart McIntosh** (Consultant Breast Surgeon, Belfast City Hospital, Belfast);
**Mrs Claire Phelan** (Clinical Nurse Specialist, Royal Free Hospital, London)

**Mr Henry Cain** led a multidisciplinary panel discussion focusing on neo-adjuvant chemotherapy (NAC) and the importance of identifying eligible patients. In his presentation he highlighted the existing guidelines for NAC eligibility and emphasised the importance of cancer biology in the identification process. This focus on biological cancer analysis has shifted the use of NAC from the preserve of locally advanced inflammatory cancers requiring downstaging for surgery, to using NAC on operable, early-stage breast cancers. The panel and the attendees were presented with a patient case study to discuss different treatment pathways.

## Fictional Case Study: Vicky

- **35 year old female**
- **T2, N0, Grade 3**
- **ER2 PR0 HER2 -ve**
- **Borderline operable with oncoplastic procedure**
- **No FHx**

## Audience Poll Results



**Presented with this patient:**

- **82% of attendees would definitely opt for NAC**
- **84% would choose EC/carbo Taxol as chemo regimen**

The panel discussed some of the barriers keeping healthcare professionals (HCPs) from opting for NAC. One such reason is that many patients do not want initial chemotherapy, as they just want the cancer removed. Mrs Phelan explained that open communication with patients is key. Patients need to be educated on why NAC is beneficial, how it links to their potential for surgery and outcome benefits. Many patients fear chemotherapy. Information needs to be given in a clear, positive and easily understandable manner to instil confidence in the treatment. In most diagnostic pathways, patients will be seen by a surgeon first. Mr Cain highlighted the importance for surgeons to discuss the benefits of NAC with their patients from the initial consultation. Dr King emphasised that every patient that matches the eligibility criteria on paper and is fit should be referred for an oncological consultation.

The treatment landscape for cases like this has changed drastically in the last few years. Dr King highlighted that 5 years ago FEC-T would have been the regime of choice. Today, 84% of attendees favour EC/carbo Taxol. The panel agreed that this shift has occurred based on the BrighTNEss trial[1], which showed that the addition of carboplatin to paclitaxel not only improved the pathological complete response (pCR) but also the event-free survival (EFS) compared to the control without added carboplatin.



1. Loibl et al. Lancet Oncol. 2018. 19: 497-509.

## The NeST Audit

Mr Stuart McIntosh presented the results of the NeST (Neo-adjuvant Systemic Therapy) study[1] that investigated the current UK practice regarding neo-adjuvant therapy, its impact on surgical management decisions and explored the "real world" pathological response rates. The audit ran from December 2017 to November 2018 across 39 self-selected centres in the UK. The NeST patient baseline characteristics and pathology response results are highlighted in the tables below.

NeST Audit Patient Baseline Characteristics[1]

| | |
|---|---|
| Median age (range) | 51 (range 22-86) |
| Symptomatic<br>Screen-detected<br>Unknown | 774<br>141<br>1 |
| Median mammographc size (range)<br>Median US size | 30mm (0 – 152mm)<br>26mm (0 – 100mm) |
| Node negative<br>Node positive<br>Unknown | 449 (49%)<br>461 (50%)<br>6 (1%) |

NeST Audit Results: Pathological Response[1]

| | Final pathology response, n (%) | | | | | |
|---|---|---|---|---|---|---|
| | pCR | | | pPR | No response | Total |
| *Pre-treatment pathology* | *ypT0* | *ypT0/ypTis* | *ypT0/ypTis, yN0* | | | |
| **HER2+** | **166 (39%)** | **236 (55%)** | **205 (48%)** | **180 (42%)** | **10 (2%)** | **426 (46%)** |
| **TNBC** | **89 (34%)** | **110 (42%)** | **101 (38%)** | **129 (49.2%)** | **23 (9%)** | **262 (29%)** |
| **ER + HER2 -** | **27 (12%)** | **34 (15%)** | **24 (10%)** | **175 (77%)** | **19 (8%)** | **228 (25%)** |
| **Total** | **282 (31%)** | **379 (41%)** | **330 (36%)** | **484 (53%)** | **52 (6%)** | **916** |

Adapted from Fatayer et al. BJS. 2022. Supplementary Material

As the 39 centres that participated in this study were self-selected, Mr Cain highlighted that these centres were potentially more prone towards NAC. There are currently 111 breast cancer centres in the UK, with the NeST audit representing only a small sample of those centres. He highlighted that no denominator for these datasets exist and there is currently no way to identify how many patients actually should receive NAC based on current guidelines, and if centres are under-prescribing NAC. Without these data, it is difficult to identify a need for improvement.

Mr Cain pointed towards the need for more clearly defined guidelines for NAC identifying the right patients, who currently still slip through the system. The newly released UKBCG/ABS Guidelines[2] are a step towards more defined guidance for healthcare professionals (HCPs).

Following the existing treatment guidelines Mr Cain presented the results of the case study.



1. Fatayer et al. BJS. 2022. 109(9):800-803. Supplementary Material.
2. Palmieri et al. UKBCG. 2022.

### Best Practice Barriers

Finally, the panel discussed current barriers that may stop HCPs from following existing guidance for NAC in early-stage breast cancer patients. Mrs Phelan stated that there still are a significant number of patients that struggle with the idea of receiving chemotherapy prior to surgery. Here, psychological support is fundamental. Patients need to be encouraged to meet their oncologist, be made comfortable with the process and team supporting them, and also need to know that they can ask their healthcare team questions they are unsure about. Dr King proposed that the availability of genetic testing could potentially lead to an uptake in neo-adjuvant treatments, as patients might recognise this as a reason to change their surgical options.

Mr Cain highlighted that lack of resources can limit patient access to NAC. Often it is more difficult to find an available chemotherapy appointment for a patient, than schedule surgery.

Mr Stuart McIntosh emphasised that HCPs must move away from focusing on historical datasets regarding adjuvant vs. neo-adjuvant overall survival, which might be holding some HCPs back. Developments in biological cancer diagnostics allow for a much better patient selection. Therefore, the new evidence supports the benefits of NAC and he believes that more HCPs are coming to the same conclusion after reviewing this evidence.

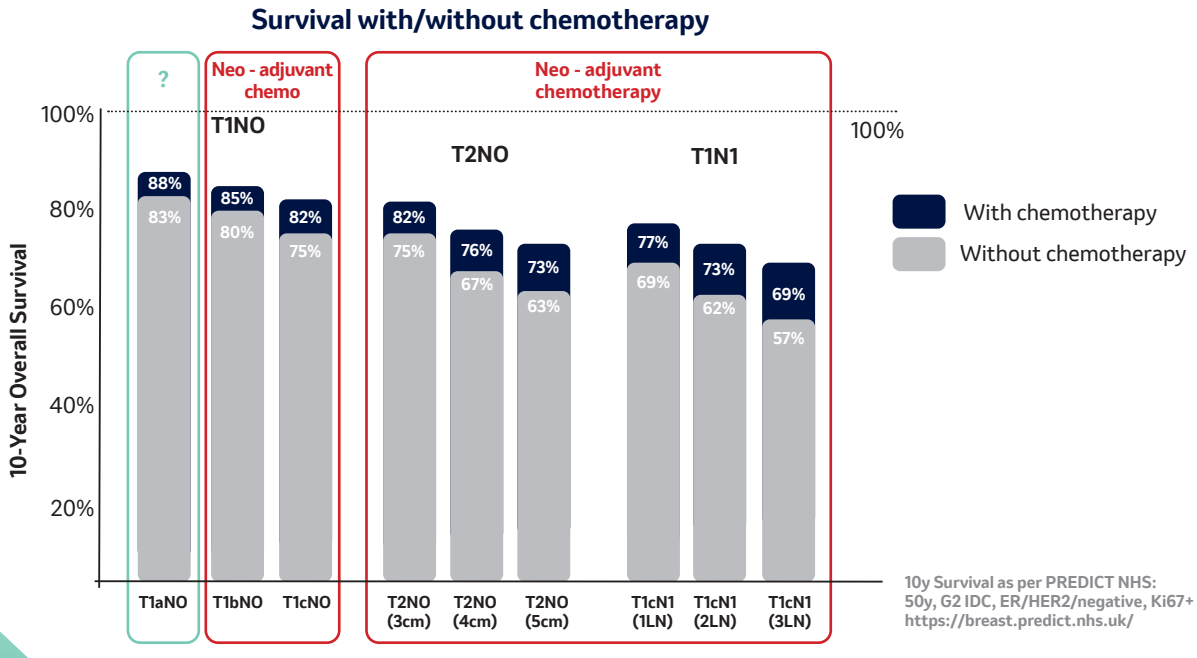
## Immunotherapy in early-stage triple negative breast cancer (TNBC)

Presented by Professor Peter Schmid, MD PhD FRCP (Consultant Medical Oncologist, Barts Cancer Institute, London)



Prof. Schmid's presentation centred around the KEYTRUDA KEYNOTE-522 data (KN-522). In his introduction, he emphasised the impact of neo-adjuvant chemotherapy (NAC) across different stages of TNBC[1], emphasising that even patients with tumours smaller than 2cm show a beneficial response.

### Do all patients with early TNBC need chemotherapy?




Adapted from Schmid et al. Presented at SABCS 2022.

1. Schmid P et al. N Engl J Med. 2020. 382: 810-821 (plus supplementary appendix)

Please click the following links for the KEYTRUDA SmPC and prescribing information: **Great Britain**; **Northern Ireland**.

Healthcare professionals must move away from referencing historical datasets, suggesting that there was no inherent benefit to neo-adjuvant therapy, as new data shows the positive impact NAC has, specifically in TNBC and HER2+ patients.

Prof. Schmid highlighted two core benefits that can derive from NAC.

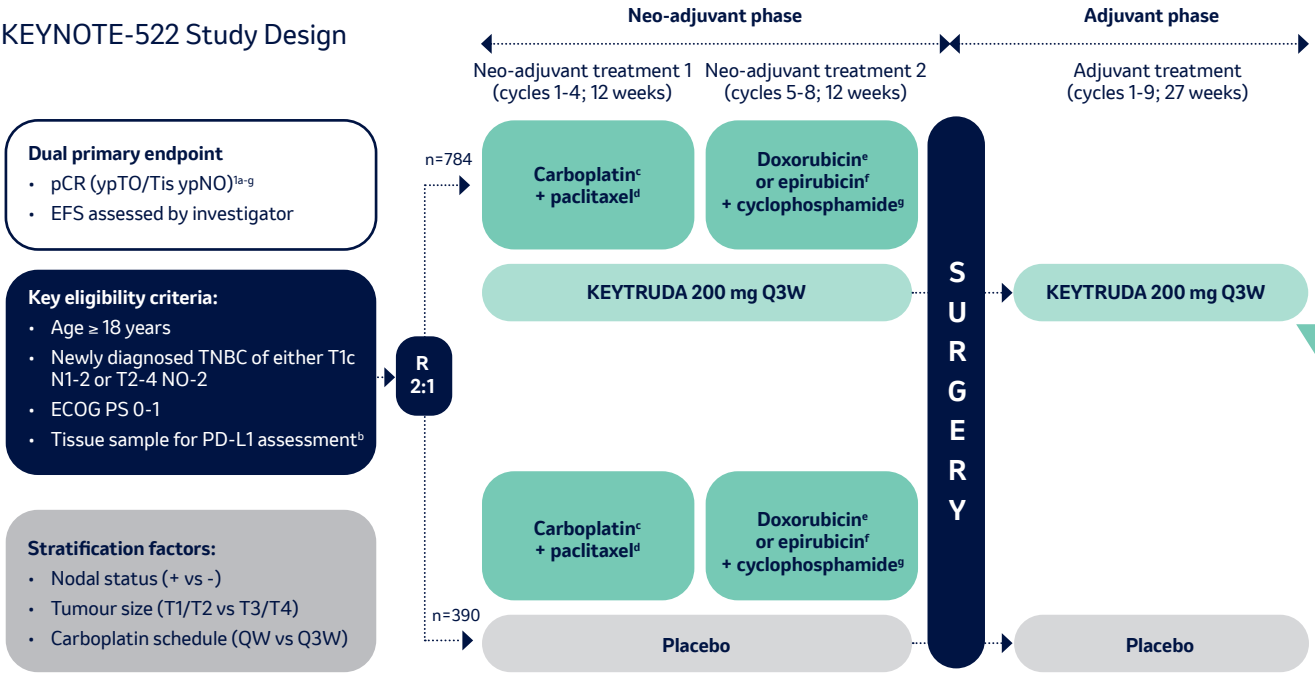
1. NAC offers the potential of downstaging the cancer for a better surgical outcome.
2. Patients receiving NAC can be divided into two groups:

    a.) Patients with pathological complete response (pCR), who show excellent outcome rates.

    b.) Patients with residual disease, whose outcome can be modified in the adjuvant treatment phase by learning from the cancers response to NAC and adapting the chemotherapy regimen.

Following his brief introduction into the current standards of NAC, Prof. Schmid moved on to present core data from the KN-522 study.

KEYNOTE-522 Study Design




Adapted from MSD KEYTRUDA Key Data Slide Deck. 2022

The KN-522 trial had dual primary endpoints, allowing for the analysis of KEYTRUDA's short-term benefits (pCR) as well as its long-term effect on outcome (EFS).[1]

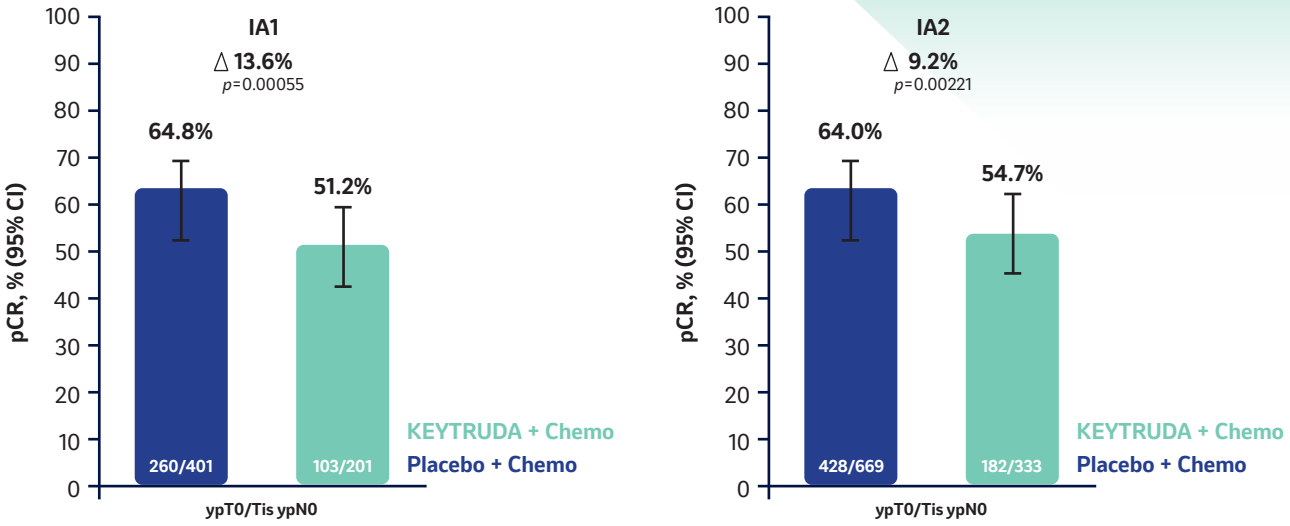
The primary endpoint analysis of the KN-522 trial highlighted that NAC[#] + KEYTRUDA showed a significant improvement in pCR compared to NAC + placebo ( IA1: p=0.00055*; IA2: p=0.00221**).[1] The KN-522 EFS data provided strong evidence that NAC + KEYTRUDA improves the patient's long-term outcome and reduces the risk of recurrence compared to the NAC + placebo group.[1]



1. Schmid P et al. N Engl J Med. 2020. 382: 810-821 (plus supplementary appendix)

## KEYTRUDA KN-522 Primary Endpoint Results[1,2]

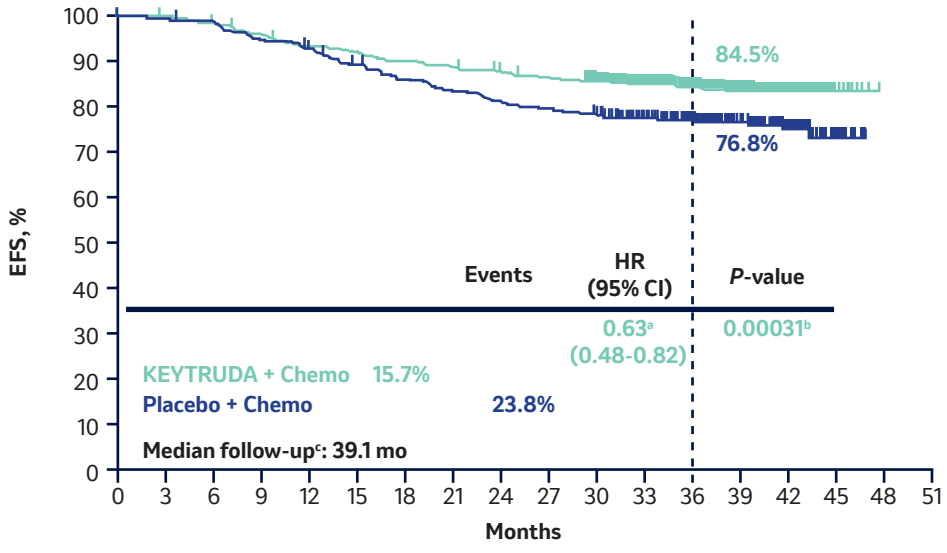
### Pathological Complete Response Rates




Adapted from Schmid et al. 2020
IA1: N=602; Data cut-off: 24 September 2018
IA2: N=1002; Data cut-off: 24 April 2019



### Event-Free Survival Rates




| No. at Risk | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| KEYTRUDA + Chemo | 784 | 782 | 769 | 751 | 728 | 718 | 702 | 692 | 681 | 671 | 652 | 551 | 433 | 303 | 165 | 28 | 0 | 0 |
| Placebo + Chemo | 390 | 386 | 382 | 368 | 358 | 342 | 328 | 319 | 310 | 304 | 297 | 250 | 195 | 140 | 83 | 17 | 0 | 0 |

Adapted from Schmid et al. NEJM 2022

# NAC in KN-522: 12 wks carboplatin/paclitaxel followed by 12 wks doxorubicin or epirubicin + cyclophosphamide
* Interim Analysis 1: N=602; Data cut-off: 24 Sep. 2018
**Interim Analysis 2: N=1002; Data cut-off: 24 Apr. 2019

1. Schmid P et al. N Engl J Med. 2020. 382:810–821 (plus supplementary appendix).
2. Schmid P et al. N Engl J Med 2022;386:556–567.

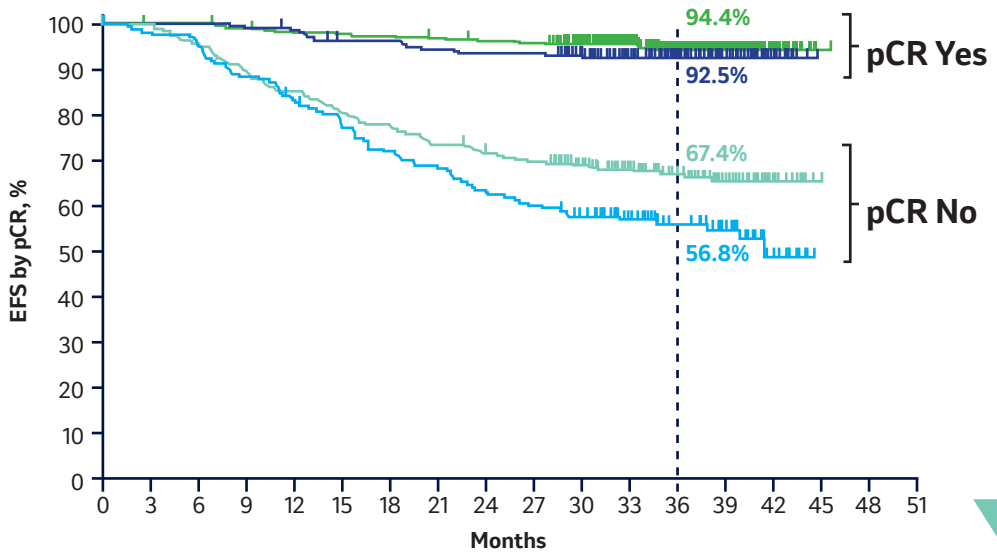
Please click the following links for the KEYTRUDA SmPC and prescribing information: **Great Britain**; **Northern Ireland**.

Exploratory analyses of core subgroups included in the KN-522 trial suggest that NAC + KEYTRUDA can have a potential benefit for both, N0 and N+ patients. While more N+ patients achieve pCR, both N+ and N0 patients show similar EFS rates compared to patients treated with NAC + placebo, suggesting a positive impact NAC + KEYTRUDA on long-term outcome for both patient groups.[1]

Patients that achieved pCR during KN-522 showed high EFS rates, no matter if they received KEYTRUDA, or placebo. Importantly, patients that did not achieve pCR after receiving NAC + KEYTRUDA, who would normally be considered to have failed treatment, still had a suggested improvement in EFS compared to patients that received NAC + placebo.

**Event-free survival by pCR**

KN-522 was not powered to detect differences between subgroups and no conclusions should be drawn from this analysis.




| No. at Risk | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| KEYTRUDA + Chemo Responder | 494 | 494 | 494 | 489 | 483 | 482 | 487 | 477 | 472 | 470 | 460 | 387 | 220 | 122 | 18 | 0 | 0 | 0 |
| Placebo + Chemo Responder | 217 | 217 | 217 | 216 | 214 | 297 | 296 | 203 | 299 | 200 | 197 | 165 | 87 | 56 | 9 | 0 | 0 | 0 |
| KEYTRUDA + Chemo Non-Responder | 290 | 287 | 275 | 262 | 245 | 236 | 224 | 215 | 209 | 201 | 192 | 164 | 83 | 43 | 19 | 0 | 0 | 0 |
| Placebo + Chemo Non- Responder | 173 | 169 | 165 | 152 | 144 | 135 | 122 | 116 | 110 | 104 | 100 | 85 | 53 | 27 | 88 | 0 | 0 | 0 |

Adapted from Schmid et al. NEJM. 2022.

Hence, the KN-522 data suggests that adding KEYTRUDA to NAC can improve the patient's long-term outcome and reduce the risk of recurrence, whether pCR is achieved or not.[1,2]

To conclude his presentation, Prof. Schmid looked to the future of immunotherapy in the treatment of early-stage TNBC, by presenting a number of future trials that will investigate the potential impact of the position of immunotherapy within the treatment pathway.



1. Schmid P et al. N Engl J Med. 2020. 382:810–821 (plus supplementary appendix).
2. Schmid P et al. N Engl J Med 2022;386:556–567.

# Individualising Care for early TNBC patients

**Chair: Dr King** – (Consultant Medical Oncologist, Royal Free Hospital and Barnet Hospital London)
Panel: Mr Cain (Consultant Oncoplastic Breast Surgeon, Royal Victoria Infirmary, Newcastle Upon Tyne);
Professor Schmid (Consultant Medical Oncologist, Barts Cancer Institute, London);
Dr Wheatley (Consultant Clinical Oncologist, Royal Cornwall Hospital NHS Trust).

Dr King chaired an interactive panel case discussion focused on the individualisation of cancer care for early TNBC patients. She presented 6 case studies to the panel and the audience for discussion. The audience participated in this session via a digital polling platform.

The panel discussion focused on barriers that keep the practitioner from confidently recommending NAC + Keytruda. Prof. Schmid stated that all patients eligible, based on the KN-522 criteria, should be offered NAC + Keytruda and raised the question of how practitioners would justify not offering a treatment that can reduce the chance of cancer recurrence by 40%. Dr King suggested that barriers include capacity issues for chemotherapy, but also insecurities around the data as well as the eligibility criteria. Dr Wheatley emphasised that often, the patients themselves are not keen on chemotherapy. Prof. Schmid stated that normally, oncologists are keen to widen the group of patients that can receive a specific treatment, however, when it comes to immunotherapy, there seems to be a move backwards, trying to reduce the number of patients that receive it. He emphasised that the discussion should revolve more around de-escalating chemotherapy rather than reducing eligibility for immunotherapy.



Another discussion point revolved around ER3 cancers. One eligibility criterion for KN-522 was ER0. The panel discussed the option of taking an additional biopsy to assess the tumour for heterogeneity. Prof. Schmid pointed out that whether a patient is considered to have TNBC is decided within the MDT. Dr Wheatley highlighted that the entire biology of the patient's cancer needs to be considered to ascertain therapy benefits. Additionally, both Prof. Schmid and Dr Wheatley pointed out that biological definitions and guidelines are constantly subject to change.

The panel also discussed the impact of pre-existing, auto-immune diseases on treatment with NAC + Keytruda. Dr King emphasised that pre-screenings for hepatitis, HIV and significant cardiovascular disease in the last 12 months prior to treatment are important.

Looking at a case study of metaplastic disease, the panel discussed the concern that a lot of surgeons and patients share, which is the closing of the surgical window in patients with fast progressing disease. Prof. Schmid emphasised that this risk can be minimised by surgeons and oncologists working closely together. He highlighted that it is beneficial to offer NAC to these patients to be able to ascertain how the cancer responds to chemotherapy before surgery. By closely supervising the patient throughout neo-adjuvant treatment, the risk of the surgical window closing can be minimised, and disease progression can be caught early.

Finally, the panel discussed clinic capacity and resources as a potential barrier to the implementation of NAC + Keytruda. Mr Cain emphasised that his centre conducts research on the impact of implementing NAC and posed the question of what impact adding Keytruda has to the services. He highlighted that it is important to gather empirical data around how many outpatient appointments will be required and how long it takes to compound and administer drugs, to allow for the appropriate resources to be assigned. The panel agreed that there needs to be an internal push for the needed resources and a review of current cancer treatment protocols.

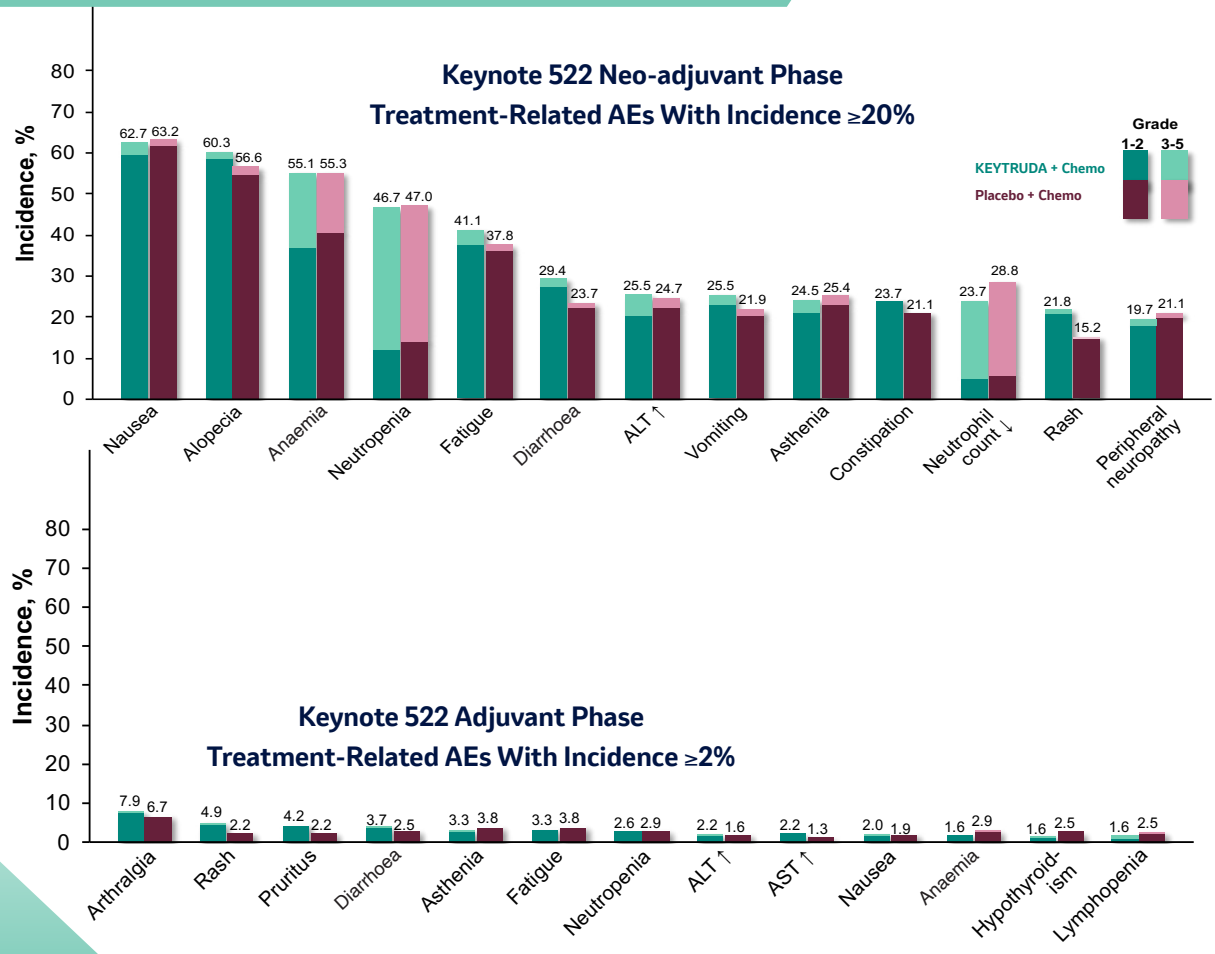
# Identification and management of immunotherapy related adverse events

**Chair: Dr Phillips** – (Consultant Medical Oncologist, Barts Cancer Institute);
Dr Raja (Consultant Medical Oncologist, University College London Hospitals NHS Foundation Trust);
Dr Wheatley (Consultant Clinical Oncologist, Royal Cornwall Hospital NHS Trust)

Dr Phillips gave a presentation on the concerns around toxicity management for immunotherapy. While chemotherapy related toxicity is well understood amongst HCPs, immunotherapy toxicity is still a factor many HCPs are not comfortable with. Immunotherapy toxicity is considered unpredictable, variable in time of appearance and can affect any organ. Immunotherapy may lead to immune-related adverse events (auto-immune reactions) which can show in a variety of ways. (Please consult the Keytruda SmPC for information on how to manage irAEs.)

Dr Phillips presented data from the KN-522 study on adverse events and highlighted that the incidence of treatment related adverse events was greater in the neo-adjuvant phase than in the adjuvant phase because the majority of AEs are linked to the chemotherapy component of the treatment.

## Neo-adjuvant Chemotherapy: Treatment-Related Side Effects




Adapted from Schmid et al. NEJM. 2020



1. Schmid P et al. N Engl J Med 2020;382:810–821.
2. Schmid P et al. ESMO 2019.
3. Keytruda (pembrolizumab) Summary of Product Characteristics. Available at: https://www.medicines.org.uk/emc/product/2498/smpc#gref. Accessed January 2023.

Please click the following links for the KEYTRUDA SmPC and prescribing information: **Great Britain**; **Northern Ireland**.

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When reviewing the adjuvant AE data, it can be seen that the number of adverse events is much lower than in the neo-adjuvant phase, with the main AEs being infusion reactions and hypothyroidism. Dr Phillips also emphasised that the timing for immunotherapy toxicities is highly variable. Adverse events can occur after the treatment has ended.

Following Dr Phillips' presentation, Dr Raja and Dr Wheatley presented six patient case studies focused on common adverse events linked to immunotherapy, like hypo/hyperthyroidism and skin rashes. Dr Raja and Dr Wheatley highlighted the best course of action for each case study and emphasised some of the pitfalls that can be encountered. Dr Wheatley heavily emphasised the importance of working in an interdisciplinary way when managing adverse events, allowing oncologists to learn from treatment protocols originating in fields like dermatology, endocrinology and gastroenterology.

Dr Raja highlighted that patient education cannot be neglected. Patients have to be made aware that AEs can occur long after the last course of therapy and have to be encouraged to communicate these to doctors that are not directly involved in their cancer care (e.g. urgent care/emergency department staff). Their oncologist should be notified if the patient attends urgent care, in order to prevent misdiagnosis and inadequate treatment.

Dr Phillips emphasised that it is of key importance to pick up adverse events early to allow for prompt intervention so patients can continue with their cancer therapy. The panel agreed that the more experienced HCPs become in managing irAEs, the more comfortable they will become in managing them.



# Workshop 1: Optimising adverse event management pathways

**Chair: Dr King** (Consultant Medical Oncologist, Royal Free Hospital and Barnet Hospital, London)
Dr Phillips (Consultant Medical Oncologist, Barts Cancer Institute)

Dr King and Dr Phillips ran an interactive workshop focused on further investigating adverse event management for immunotherapy. Using two previously presented case studies, Dr Phillips and Dr King opened the floor for questions from the attendees, as well as encouraging the attendees to share experiences across centres. Dr Phillips emphasised the importance of this type of conversation between practitioners as a lot of concern still exists surrounding the introduction of Keytruda. While the Keytruda data are showing outcome improvement to both pCR and EFS when added to the existing cancer therapy regimen, centres must focus on guiding their medical teams on how to manage these new AEs and educate their MDTs on the new management pathway. The attendees pointed out that this education should extend to patients as well. Most patients refer to any kind of cancer treatments as chemotherapy, which then leads to misdiagnosis and mistreatment in urgent care and emergency departments. Patients may receive corticosteroids too late, in too low doses or not for long enough, leading to recurrence of symptoms. Patients need to be made aware that immunotherapy is different from chemotherapy and that side effects

can occur even after the treatment has stopped.

Another area of discussion was corticosteroid dosing. Dr King recommended to start patients on a high corticosteroid dose (2mg/kg) and then slowly reduce the dosing when a symptom reduction can be observed. AEs should be at Grade 1 before restarting therapy. She emphasised that the administration of steroids can lead to confrontations with other practitioners not used to treating immunotherapy adverse events, as in some cases corticosteroid treatment can be counterintuitive (e.g. heavy colitis that could be interpreted as septic, requiring antibiotics). Here it is important to educate other HCPs on the right approach to dealing with immunotherapy adverse events.

Dr Phillips highlighted that while Acute Oncology Services (AOS) guidelines for managing IO adverse events exist, not all healthcare professionals are aware of that. Dr King emphasised NAC without IO also carries significant side effects, however, as practitioners are more familiar with them, they are less wary; it is important to always view the risks of a therapy in relation to its benefits.

The workshop attendees suggested that adding speakers from areas like dermatology, gastroenterology, as well as oncologists focusing on lung and melanoma care to these meetings could offer a different perspective on AE management.

## Workshop 2: Optimising management of the axilla post neo-adjuvant treatment



**Chair: Dr Wheatley** (Consultant Clinical Oncologist, Royal Cornwall Hospital NHS Trust)
Mr McIntosh (Consultant Breast Surgeon, Belfast City Hospital)

In the beginning of this workshop, Mr McIntosh took his participants back to axillary management options prior to neo-adjuvant therapy, which focused on a radical surgery approach. He emphasised the drastic shift the field is seeing now that data have become available that clearly shows the correlating benefit of neo-adjuvant therapy for breast and axillary treatment. He posed the question to the workshop attendees "if axillary conservation is possible in a patient with node positive disease, why would you not?" Mr McIntosh presented an excerpt of the surgical data collected during the UK NeST Study[1] to the audience. The data showed surgical downstaging to be less common in the axillar and axillary re-assessment is not routinely performed. Additionally the study showed that 65% of cN+ve patients underwent axillary clearance which can cause a variety of long-term negative effects. Almost 50% of these patients had no residual axillary disease at time of surgery.

Mr McIntosh emphasised that it is key to do better for these patients. He highlighted that new studies have shown the ability to downstage the axilla, followed by sentinel lymph node biopsy (SLNB), allowing for the possibility to conserve the axilla. In cases where patients were found to have residual axillary disease, axillary clearance is still required, and studies are focusing on the best options for these patients.

Dr Wheatley provided the participants with an overview of different non-surgical approaches to manage cN+ve patients prior to surgery. He presented a summary of the AMAROS study, [2,3] which randomised cN+ve patients into axillary radiotherapy or axillary lymph node dissection, as well as the NEOSENTITURK

1. Fatayer et al. BJS. 2022. 109(9): 800-803.
2. Rutgers E. et al. SABCS 2018. Abstract (GS4-01).
3. Donker, M., et al. Lancet Oncol. 2014; 15(12); 1303-1310.

trial.[1] He emphasised that these studies show a trend that when patients can be cured with chemotherapy, radiotherapy is unnecessary, and the recurrence rates are very low. One of the workshop attendees highlighted that their centre lacked radiology capacity, and that they do not tend to mark their nodes at the current stage.

Dr Wheatley and Mr McIntosh both encouraged attendees to implement marking into the protocol, as it has a positive impact on the patient. A question that was posed to the panel was to define the difference of targeted axillary clearance in comparison to other surgical approaches. Mr McIntosh explained this process to be a scientifically guided identification of removable nodes, using nodal marking as a guiding point for surgery.

Following some audience questions, Mr McIntosh emphasised that there is still need for Level 1 RCT evidence to make people comfortable with the existing management pathway, which is why he supports the implementation of ATNEC.[2]

## Workshop 3: Optimising conversations with the younger TNBC patient

**Chair: Dr Raja** (Consultant Medical Oncologist, University College London Hospitals NHS Foundation Trust), Mr Cain (Consultant Oncoplastic Breast Surgeon, Royal Victoria Infirmary, Newcastle Upon Tyne) Mrs Phelan (Clinical Nurse Specialist, Royal Free Hospital and Barnet Hospital, London)

In this workshop, the panel opened with a conversation about fertility in TNBC patients and the obstacles these patients can face during their cancer treatment. Dr Raja posed the question of when and how to discuss fertility with a newly diagnosed TNBC patient and asked the panellists what they recommended as the first step in starting a conversation. Mrs Phelan recommended having this discussion as early as possible in the patient pathway and to focus on the patient's holistic needs. She emphasised the importance of identifying a support system for the patient to make them feel comfortable and open to these types of conversations. Mr Cain pointed out that the initial concern for many patients that are diagnosed with breast cancer is losing their breast and having to go through chemotherapy. While he agreed that an early conversation about fertility is beneficial he believes that it is important to give patients time to reflect and come to terms with their diagnosis before focusing on its impact on their fertility.



Dr Raja provided an overview of fertility options available. She also emphasised that a continuous dialog with the patient can help in streamlining the process of fertility preservation and chemotherapy.

Using the results from multiple retrospective studies, Dr Raja argued that despite the importance of fertility for women, conversations are often missed. Dr Raja and Mr Cain introduced the idea of inherent bias from HCPs towards fertility discussions, stressing that regardless of the woman's age or tumour type, fertility should be discussed. Dr Raja reminded the audience that discussing fertility is not a choice to be made by the HCP, it is required as a part of informed consent. Suggestions were made to expand the target demographic for these conversations based on recent trends in diagnosis age, rising maternal age and increased survival rates of younger TNBC patients.

Following a summary of the POSITIVE clinical trial data[3] by Dr Raja, the workshop concluded with a message from Mr Cain and Mrs Phelan for practitioners to keep focused on patients with optimistic results as they are often outshined by the more negative cases.

1. Karanlik et al. SABCS. 2022.
2. Goyal et al. JCO. 2022. TO5615.
3. IBCSG 48-14 POSITIVE. Accessible at http://www.ibcsg.org/en/patients-professionals/clinical-trials/closed-trials/2-ibcsg-48-14-positive. Accessed January 2023

# Summary:
# Take Home Messages from the Expert Panel

**Chair: Professor Schmid,** MD PhD FRCP (Consultant Medical Oncologist, Barts Cancer Institute, London)

***Mrs Phelan*** *"Because this treatment approach is quite new, we are seeing really good results. Be positive, be open about side effects, let the patients know that CNS and the whole clinic team are there to support them. They need to know that they can approach their treatment team with issues or questions at any point."*

***Mr McIntosh*** *"It is a multidisciplinary approach to identify these patients. It is important to understand that if we are not offering patients NAC we are denying them the opportunity of surgery and tailored treatment, which limits their long-term outcome and treatment options."*

***Dr King*** *"If you treat early breast cancer and early adjuvant patients, you will every so often get your fingers burned. That does colour your experience. One bad case of colitis or an adjuvant patient that dies is an absolute tragedy. I remember all of us being quite concerned when neo-adjuvant pembrolizumab came out. However with the ongoing clinical experience and the great results we are seeing we have to remind ourselves that while sometimes things go wrong, it is extremely rare and needs to be weighted against the clear benefits of the treatment. We should not deprive people of survival opportunities because we are feeling a little nervous. We all sometimes need to be 10% braver."*

***Dr Wheatley*** *"I remember speaking to one of my young patients that participated in the study. She had some complications, and she did not know what the benefit was of her participating. I told her, well actually, you helped produce a treatment that now everyone around the world can have." We need to remind ourselves that this is why we are doing these studies. We cannot conduct a study, see some improvements and then end up being scared to give the treatment to patients. It is all about considering the benefit against the risk."*

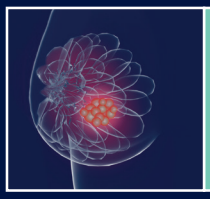
***Dr Raja*** ***"****What I learned today is that we are all hesitating mostly because of the toxicity." No one can doubt the significant benefit that can be seen. So what is holding us back? Is it adverse events? Is it the fact that our centres are too busy? As already mentioned, these reasons are unacceptable. I also think what is important is our communication. I think we forget how powerful our conversations with the patients are. If we have insecurities in a treatment, this doubt comes across, and the patient will not want to have the treatment. Therefore it is important that you are convinced, and you need to do your due diligence outside of the clinic. You need to understand what you are giving, why you are giving it and be comfortable with the toxicity management. If you are confident in a treatment, it will lead to your patient feeling confident too."*



MSD

***Mr Cain*** *"It is with great hope that we go to meetings like this one and it is not necessarily to educate and convert everyone. We like to send you back with a challenge: You need to go through MDTs and challenge your MDTs. The people here are probably not the people who need to hear all this. You came here, you are interested, you are keen to bring your service forward. We all know the situation within MDTs and sometimes it takes a great degree of bravery to stand up. You are now being empowered with the data and the knowledge to go back and challenge your MDTs. This message is reliant on people that turn up to these meetings, take the information away and do this for us."*

***Professor Schmid*** *"A lot of breast cancer patients go online searching and conclude that this is a death sentence. In the last 7 years we had four new treatments introduced that reduced recurrence rates by 40-50% compared to the existing standard therapy, with these treatments showing their benefit on top of each other. We are sometimes a little bit reluctant to see that these are big steps. For me the key message is to actually embrace the data, not just the pembrolizumab data presented today but all data, and to bring this data back to the patient. I believe patients deserve to know what the data are, so they can make an informed decision. Additionally, teamwork is absolutely critical, between the nurse teams, the oncologists and the surgeons it is critical to have that interaction to allow for the best possible care. This is also how we learn in our centres, how to deal with therapy. By constantly communicating and checking in with our colleagues"*



# KEYconversations

*in early-stage TNBC. Let's keep talking*

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