ARTIFICIAL INTELLIGENCE, CLINICAL DECISION SUPPORT AND BREAST CANCER TREATMENT

COGNITIVE ARTIFICIAL INTELLIGENCE: IBM WATSON FOR ONCOLOGY

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DISCLOSURE

- Representations and opinions expressed are solely my own and do not reflect those of any other party.
- Received no compensation from any party related to views expressed or performance of this work
- Thank collaborators: Manipal Oncology fellows, M-J. Sepúlveda M.D. Sc.D.,


Manipal Comprehensive Cancer Center
प्रज्ञानं ब्रह्म
Manipal
INSPIRED BY LIFE

ManipalHospitals
LIFE'S ON

Manipal Hospital, Bangalore

- 600 bed Quaternary care facility
- 53 specialties & 60 sub-specialties
- Ranked in the top 10 multi-specialty hospitals in India*
  *(The Week-Hansa survey 2012)
- Best hospital in Bangalore for 10 consecutive years*
  *(The Week - AC Nielsen Survey 2013)
- 1st Hospital in Karnataka, India to introduce Robotic Surgery
- NABH and NABL accredited
- ISO 9001:2000

Smart Hospital

- Triad of Technology and New evidence based access, Early adaption
- And Integration and making most Patient Friendly Hospital
- And giving world class health care

Intelligent hospital is one that works better and smarter. It's better because it's resourceful, creative, and perceptive about what patients and doctors need and it's smarter because it's astute and inventive when it comes to weaving together diverse technologies to enhance patient care.

Manipal

ManipalHospitals
LIFE'S ON

- Manipal Education
- Manipal Hospitals
- Manipal Research
- Manipal Integrated Services

Manipal Education

PURPOSE AND OBJECTIVES

- Objectives:
  - Define AI and illustrate its growth in health care.
  - Discuss selected clinical decision support system considerations.
  - Present the breast cancer concordance study.

- Purpose:

to describe concordance of treatment recommendations made by the Manipal Hospital Multidisciplinary Tumor Board (MMDT) and an AI treatment decision support system (IBM Watson for Oncology) for breast cancer in India.

Term AI origin:

AI was coined by John McCarthy, an American computer scientist, in 1956

at The Dartmouth Conference where the discipline was born.

However, there exists No standard universally accepted definition AI

Numerous definitions generally grouped into 4 system categories

- ***After describing "Systems that Think Like Humans—based on modeling cognitive functions of reasoning, inference and learning***

Background

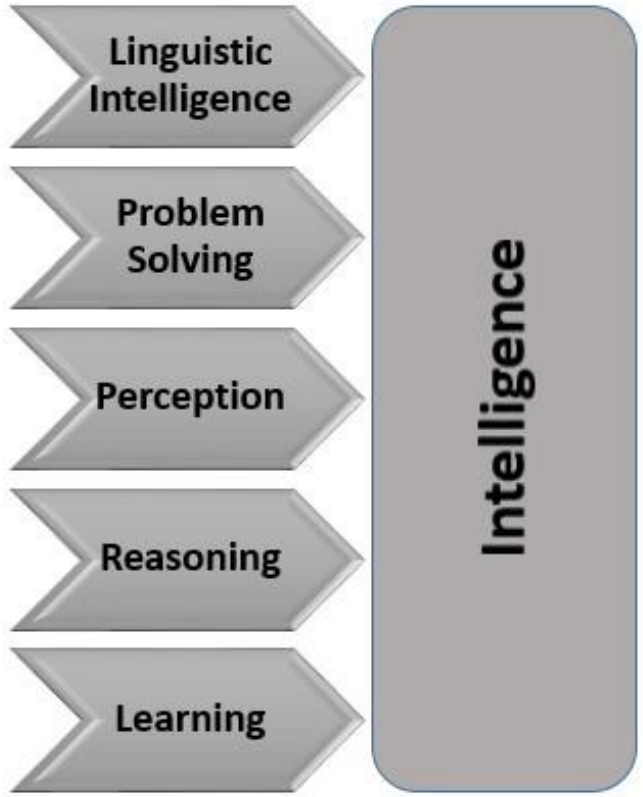
Turing Test (http://theconversation.com/person-or-computer-could-you-pass-the-turing-test-6769)

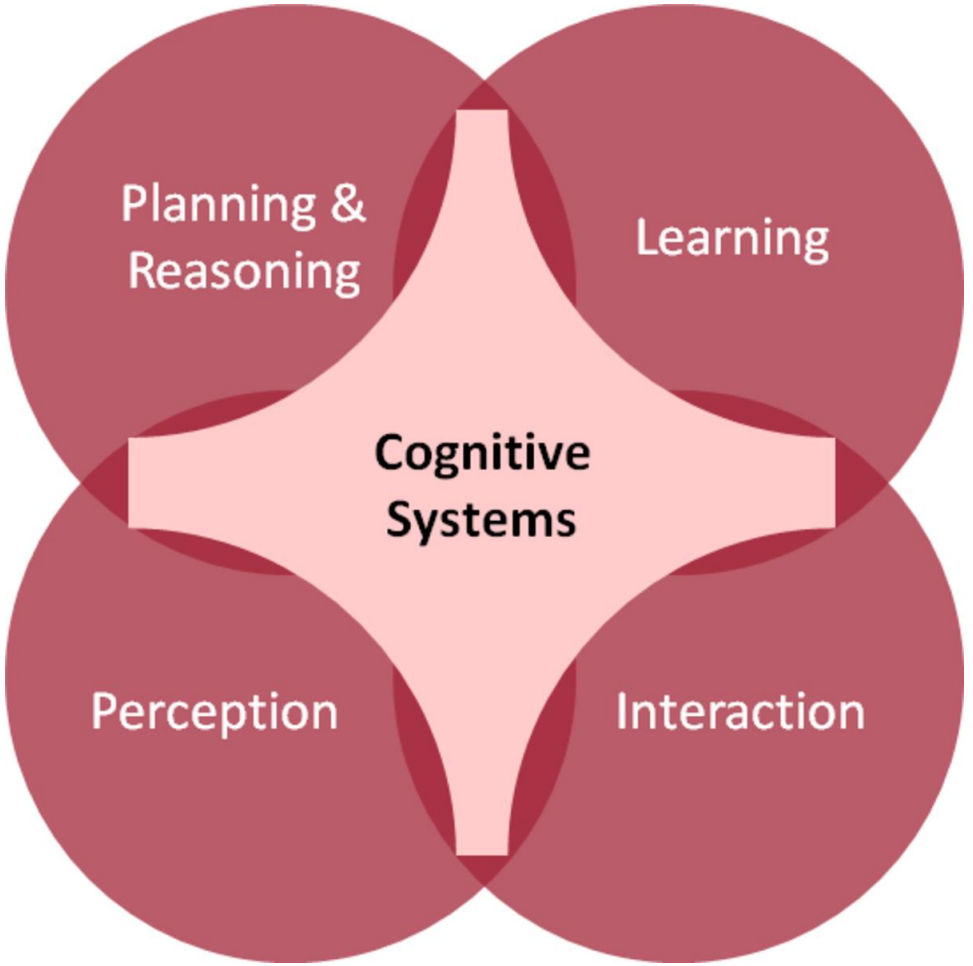
- **One of Turing's many signal contributions was a 1950 article that defined what is now known as the Turing Test.**
- **In it, he proposed a test in which a human "converses" with two entities — one human and one computer program — over a text-only channel (i.e., a computer keyboard/screen), and then attempts to determine which is the human and which is the computer.**
- **If after, say, five minutes of testing, the majority of human interrogators are unable to determine which is which, Turing said that we could claim the computer system has achieved a certain level of intelligence.**

- **Deep Blue**

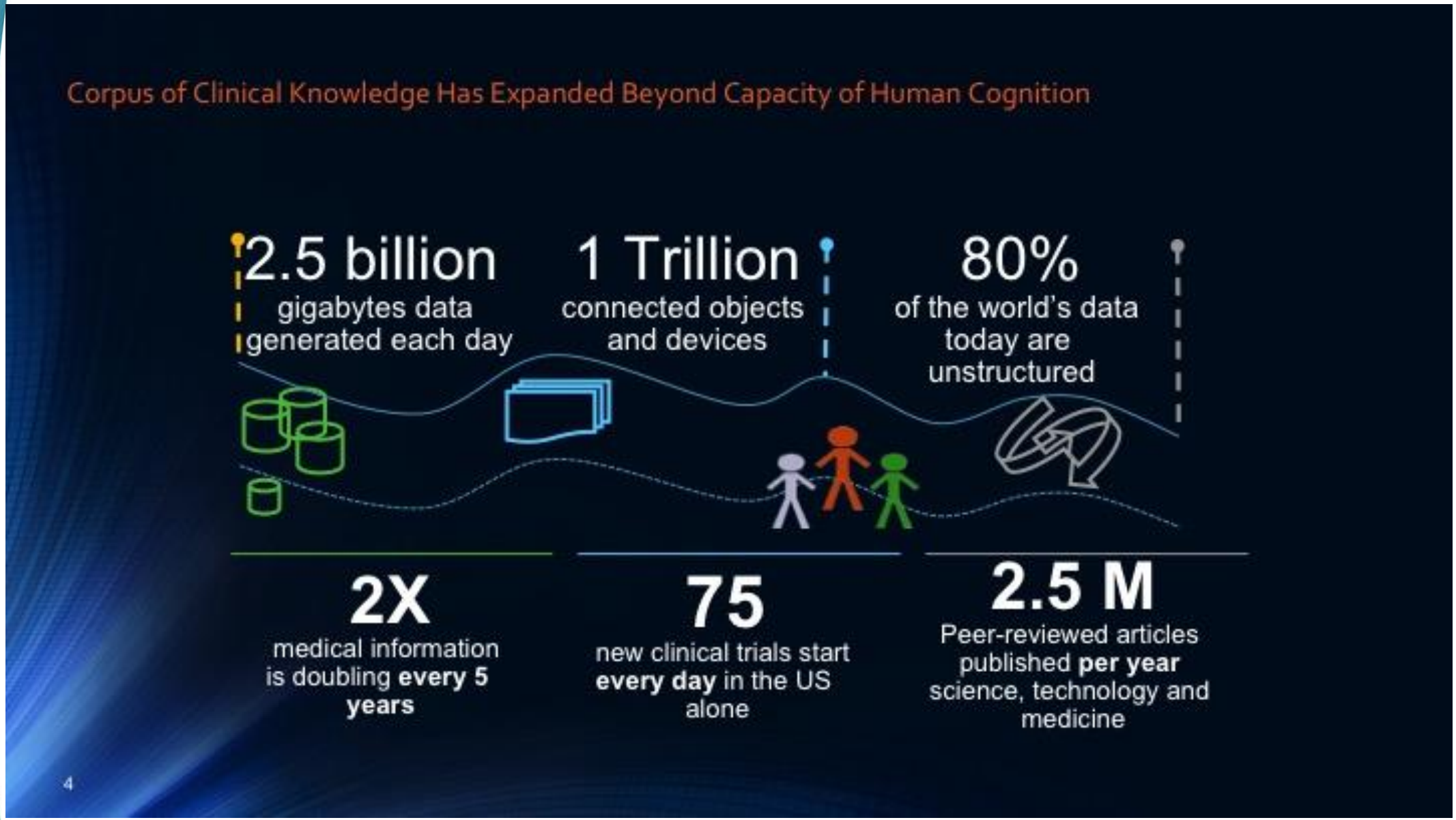
At the heart of Deep Blue's ability to play chess is its evaluation function. The evaluation function is an algorithm that measures the "goodness" of a given chess position. Positions with positive values are good for White, and conversely, positions with negative values are good for Black. If the overall score is negative, for example, this means that Black has the advantage. Deep Blue's evaluation function looks at four basic chess values: material, position, King safety and tempo. Material is based on the "worth" of particular chess pieces.
https://www.research.ibm.com/deepblue/meet/html/d.3.2.html

COGNITIVE SYSTEMS





Corpus of Clinical Knowledge Has Expanded Beyond Capacity of Human Cognition



… and vast amounts of data that can have a great impact on our health remains untapped.

Breast cancer and Oncologist

- As of Oct 2017 there are 67 approved new drugs to treat Breast cancer not including combination treatment regimens

- The growth of massive Genetic and clinical database leaves little time for accessing relevant information at point of care

A study that surveyed 1117 Oncologists, reported an average of 4.6 hours per week were spent to update and keep abreast of recent trials and drugs

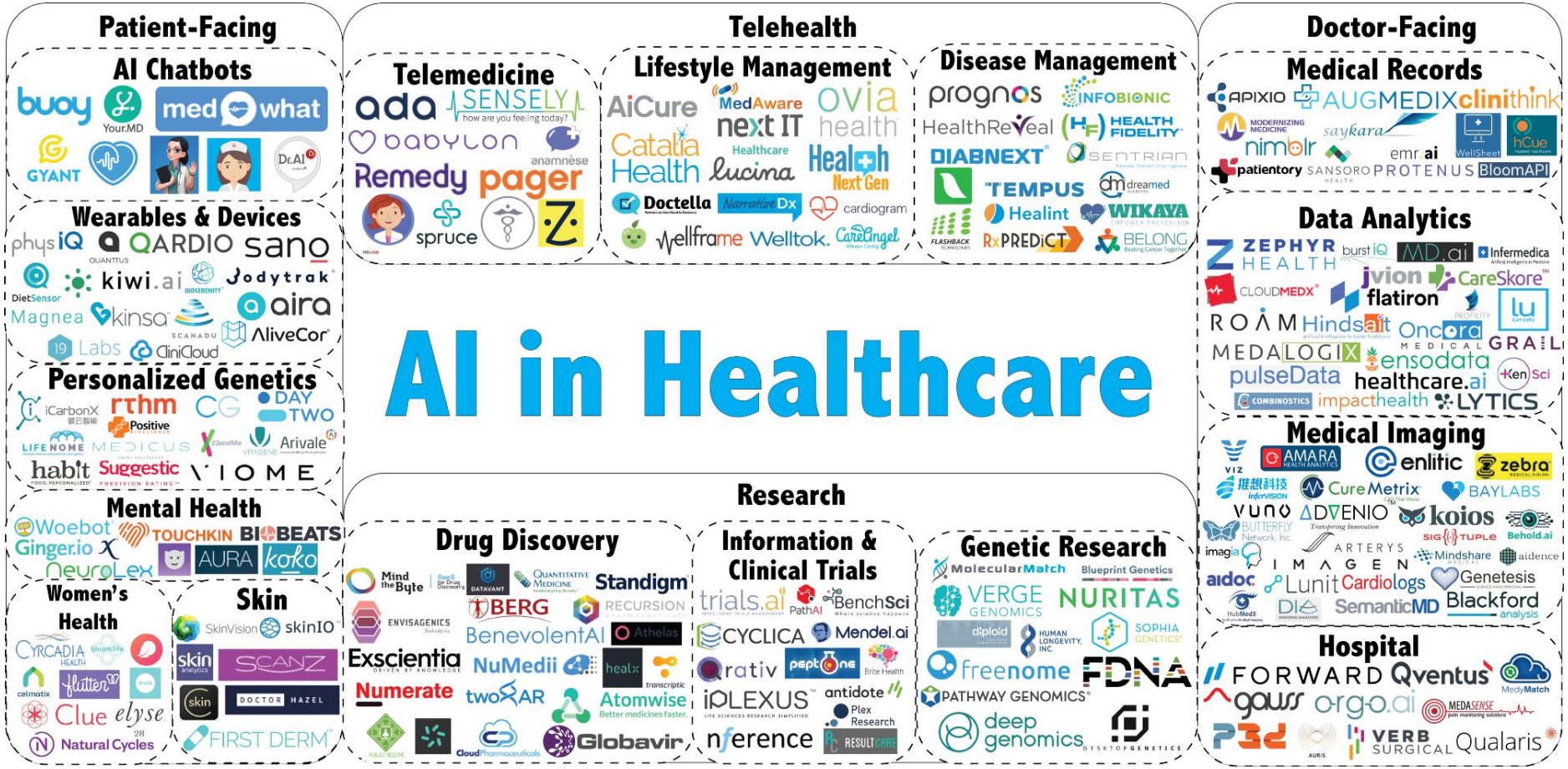
1. Seidman AD. Computer-Assisted Decision Support in Medical Oncology: We Need It Now. In ASCO Post 2016. http://www.ascopost.com/issues/april-10-2016/computer-assisted-decision-support-in-medical-oncology-we-need-it-now/ (16 December 2017, date last accessed).
2. Pusic M, Ansemmino JM. Clinical decision support systems. BCMJ 2004; 46: 236–239.

On a daily basis clinicians are challenged with…

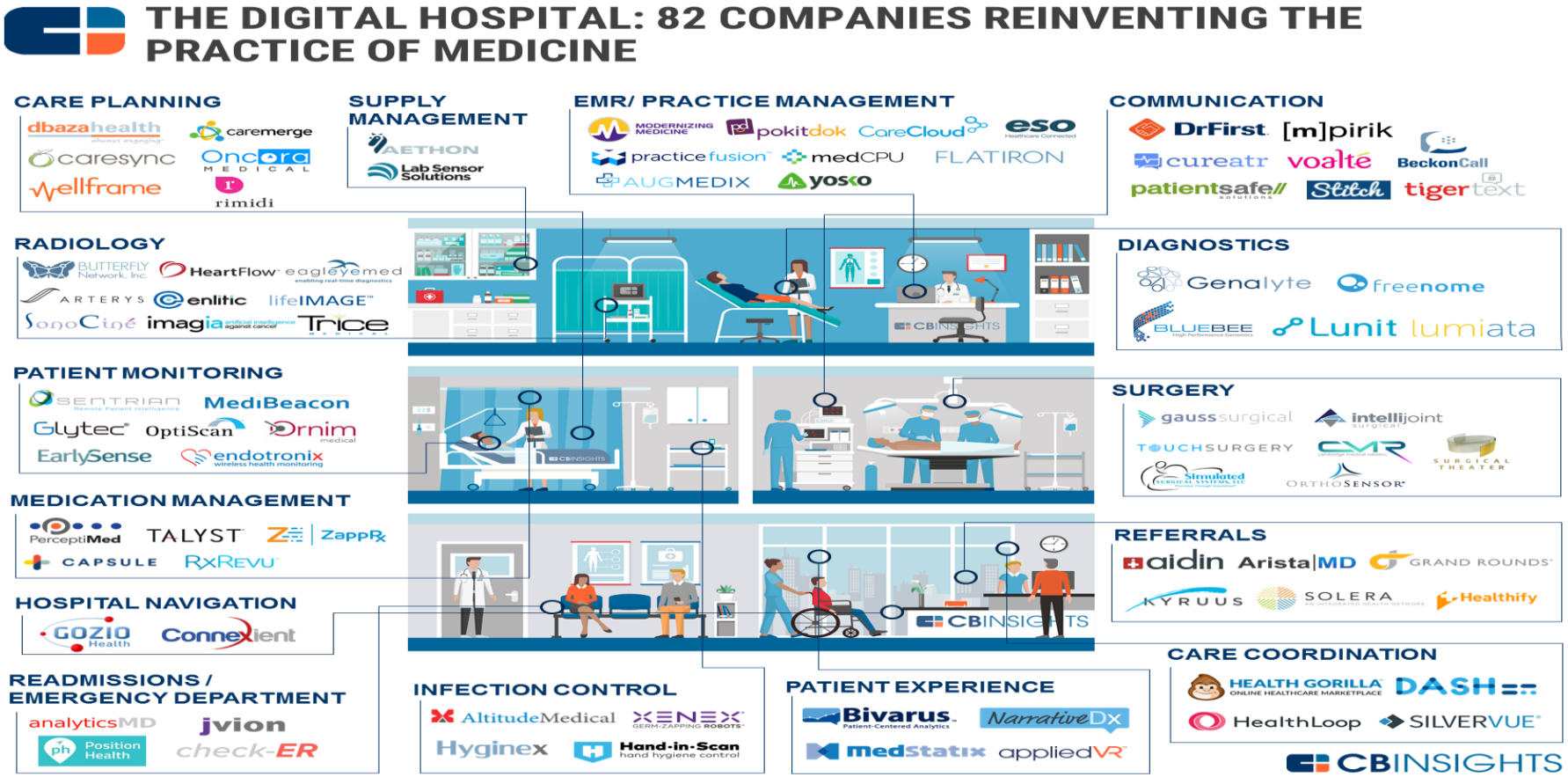
Understanding the patient condition	Formulating treatment options	Selecting personalized treatment plans
…given disparate sources and varying completeness	*…based on latest guidelines and medical literature*	*…based on comorbidities, conditions, contraindications, side effects for a patient's specific clinical attributes*

On a daily basis researchers are challenged with…

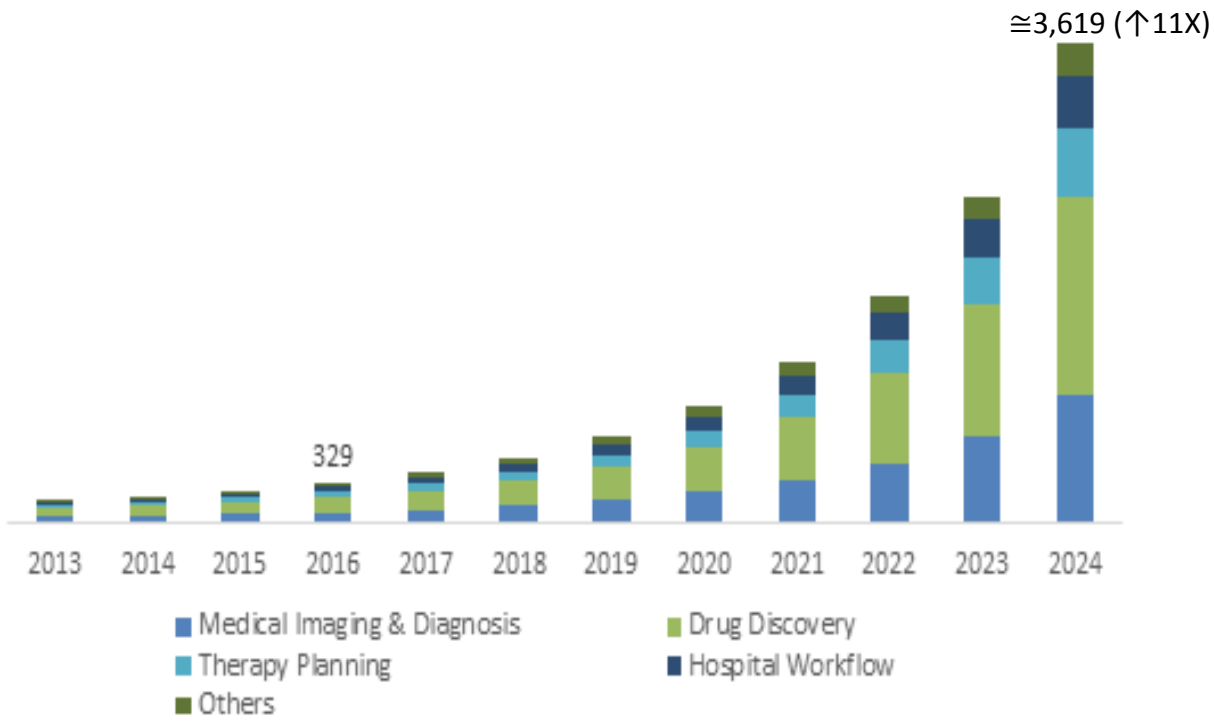
Staying up to date on research literature	Exploring and uncovering novel connections	Generating new insights for future research
…like rapidly increasing volume of research literature	*…looking across scientific domains for new relationships between diseases, genes, and drugs*	*…to develop valid hypotheses with the potential to lead to groundbreaking discoveries*



AI REINVENTING MEDICAL PRACTICE



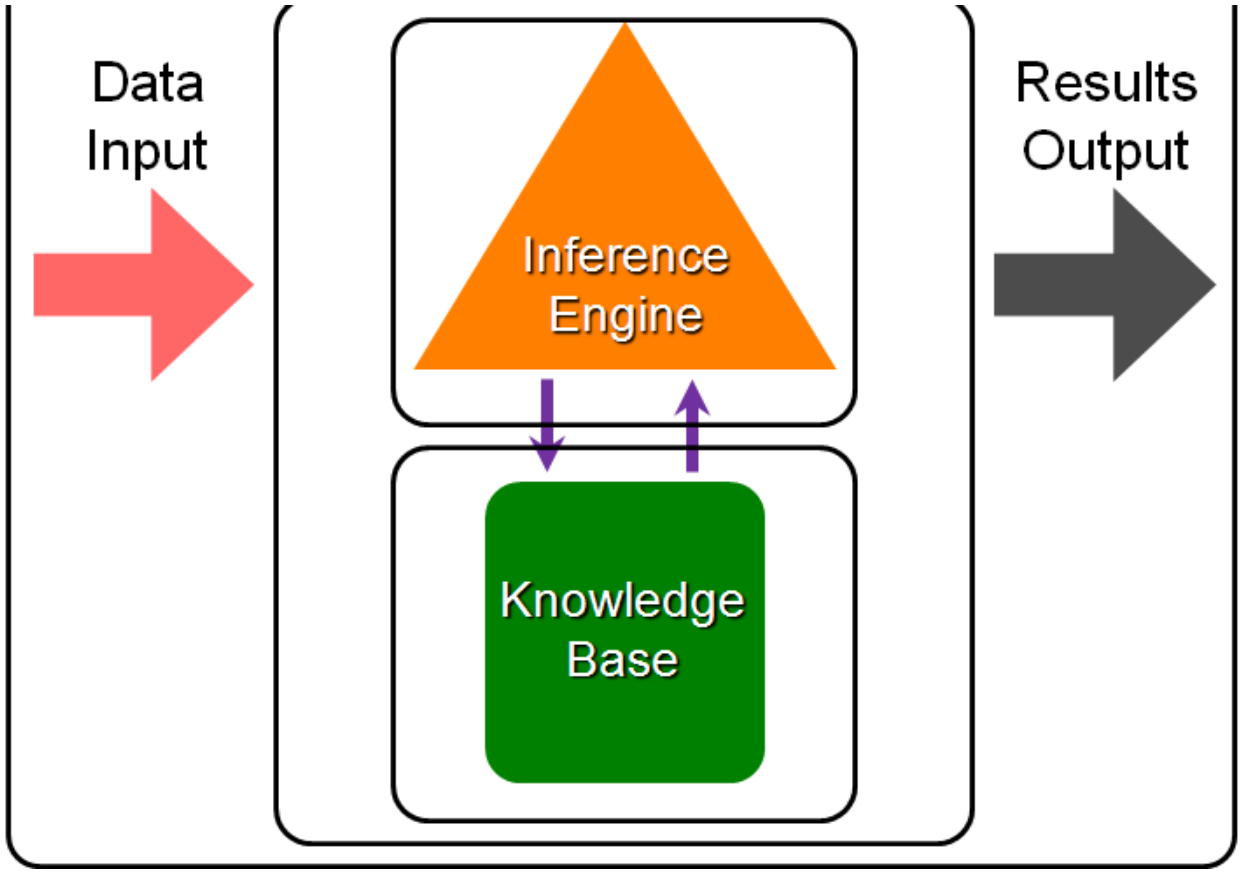
AI HEALTHCARE MARKET FORECAST, U.S. (MILLIONS US)



CDS Global Market Forecast P&S Market Research
https://www.psmarketresearch.com/market-analysis/clinical-decision-support-system-market

Cognitive Systems reason, learn and interact naturally with people to extend what humans or machines could do on their own.

AI CLINICAL DECISION SUPPORT



BATES ET AL. J AM MED INFORM ASSOC. 2003;10:523–530.
KHALIFA M. PROCEDIA COMPUTER SCIENCE 37 (2014) 422 – 427.

Adoption, Use, Value Factors

- Content: e.g. relevant, complete, current
- Information provided: e.g. valid, reliable, references accessible
- Usability: e.g. comprehensible, simple, efficient, easy to use
- Workflow integration
- EHR integration
- CDS-related Patient Safety

Selected AI CDS Evaluation Criteria

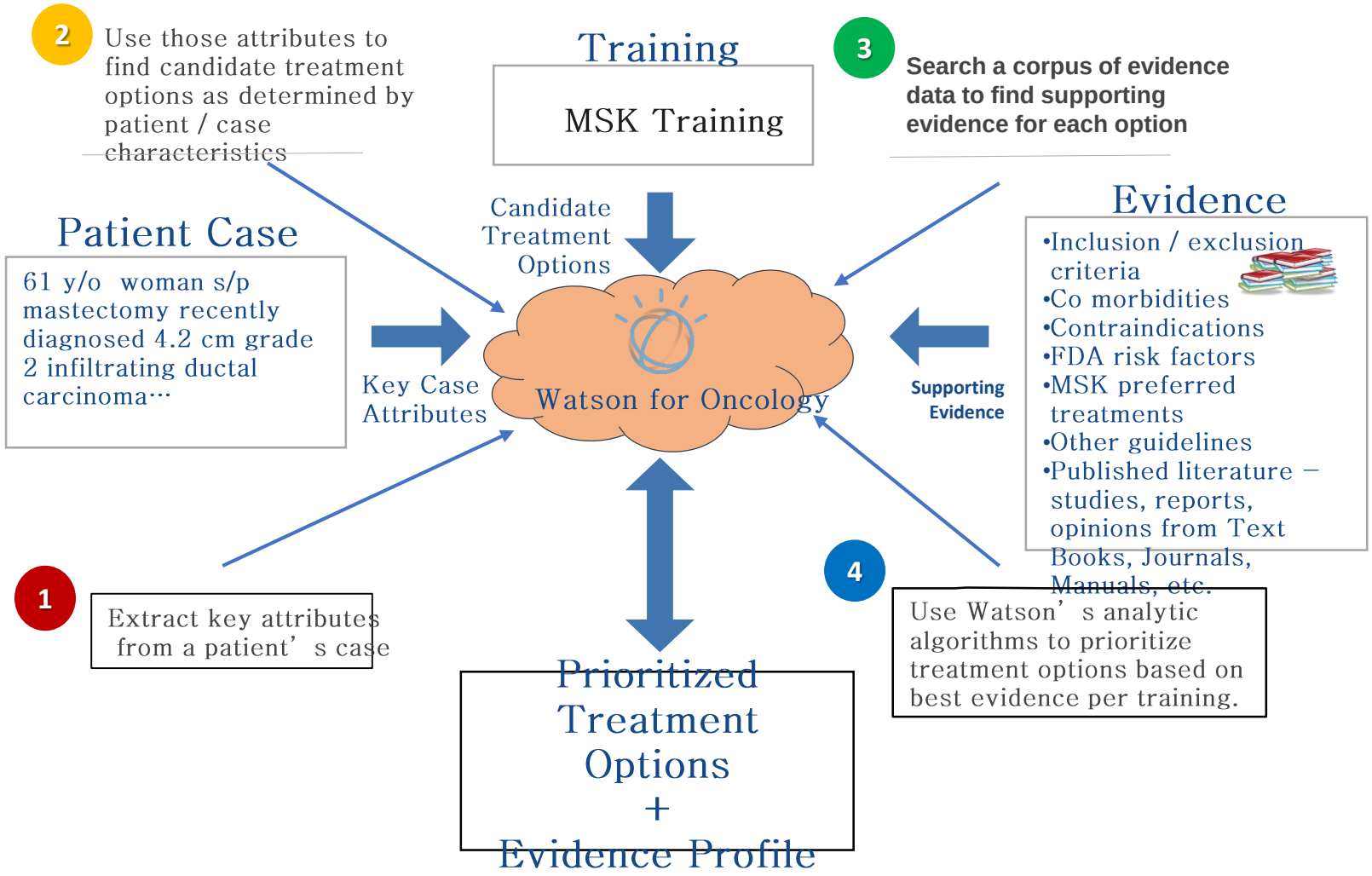
CDS are interactive computer applications that are designed to assist clinicians and other providers of care to make decisions.

Adoption, Use and Value Factors:

A CDS system must provide scientific proof, that it meets these key performance requirements with rigorous evaluation in the design, development, implementation and maintenance of the CDS.

Component	Description	Strength of Evidence
Natural Language Processing: Understanding and Supported Input Data	Structured & Unstructured Clinical Information	
	Structured & Unstructured Medical Knowledge	
	Structured & Unstructured Clinical Guidelines	
Medical Logic	Generates Attributes, inputs and Insights for the Inference Engine	
Expert Training	Coverage & Depth of Training Cases	
Usability	Comprehensibility, Ease, Simplicity, Efficiency, Accessibility	
EHR/HIS Integration	System automates data identification, abstraction, input	
Workflow Integration	Right place, time, person in natural workflow	

Watson for Oncology: How it Works

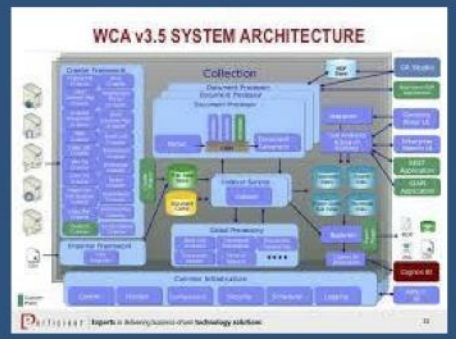


What is the Watson System?

IBM Watson is a technology platform that uses natural language processing and machine learning to reveal insights from large amounts of unstructured data.

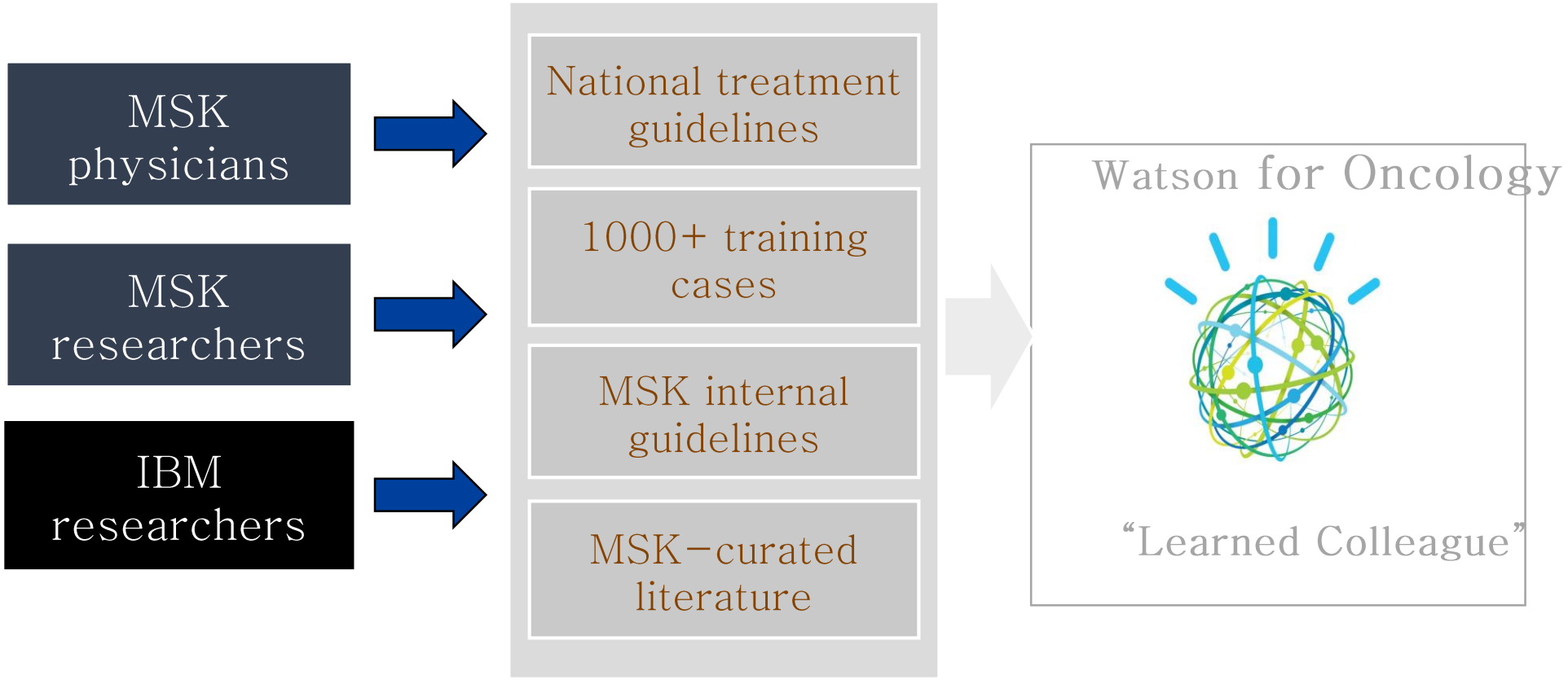
Software, Hardware, and Data

- Uses IBM's DeepQA software and Apache UIMA (Unstructured Information Management Architecture)
  - generate hypotheses, gather massive evidence, and analyze data



- Watson can process 500 gigabytes, the equivalent of a million books, per second
- Written using Java, C++, Prolog
- sources of information for Watson include encyclopedias, dictionaries, thesauri, newswire articles, and literary works

WFO Training:
Memorial Sloan-Kettering Cancer Center



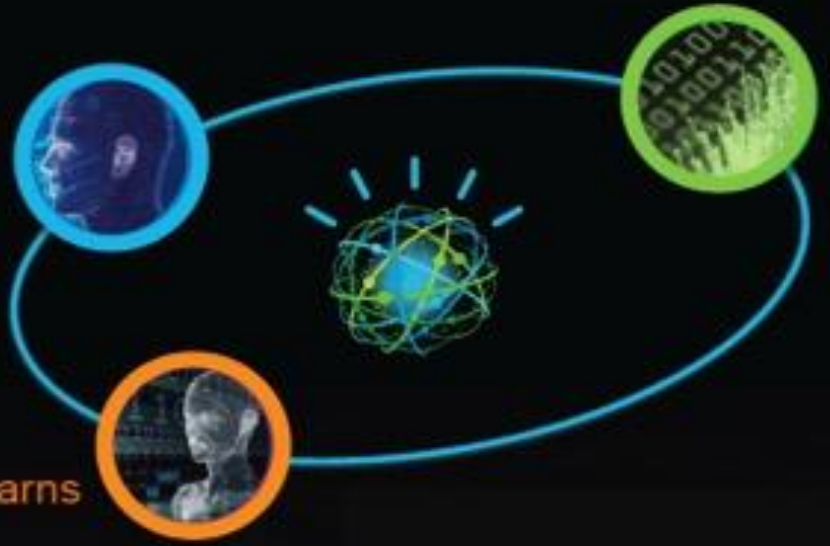
WATSON'S BACKGROUND EWADING ON ONCOLOGY

IBM Watson

1 Understands natural language and human communication

2 Generates and evaluates evidence-based hypothesis

3 Adapts and learns from user selections and responses

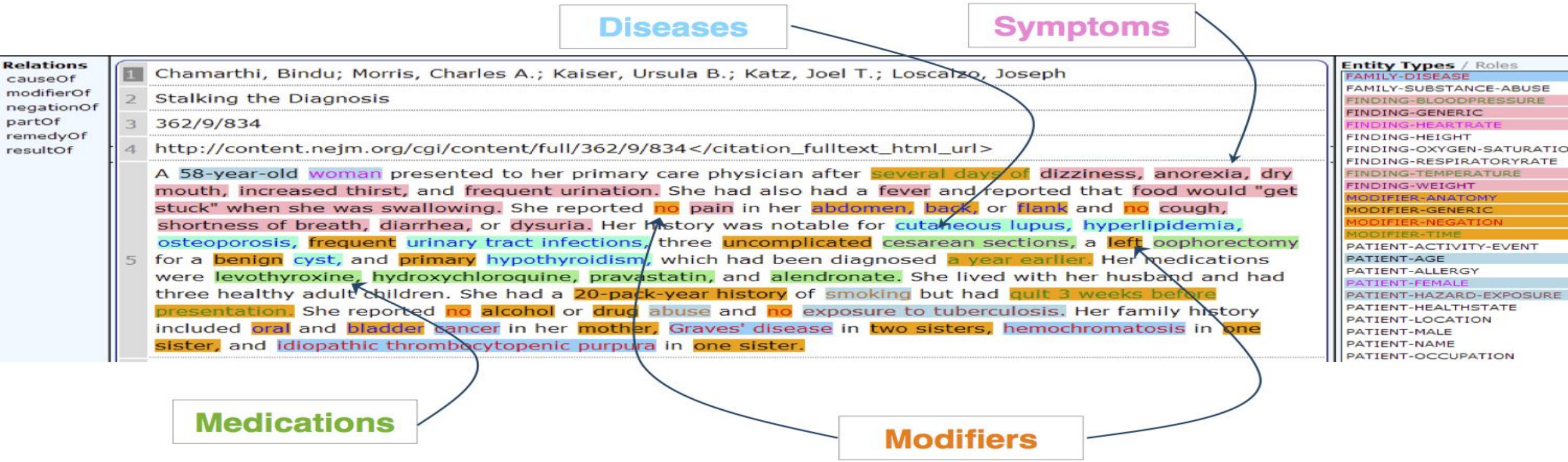


IBM

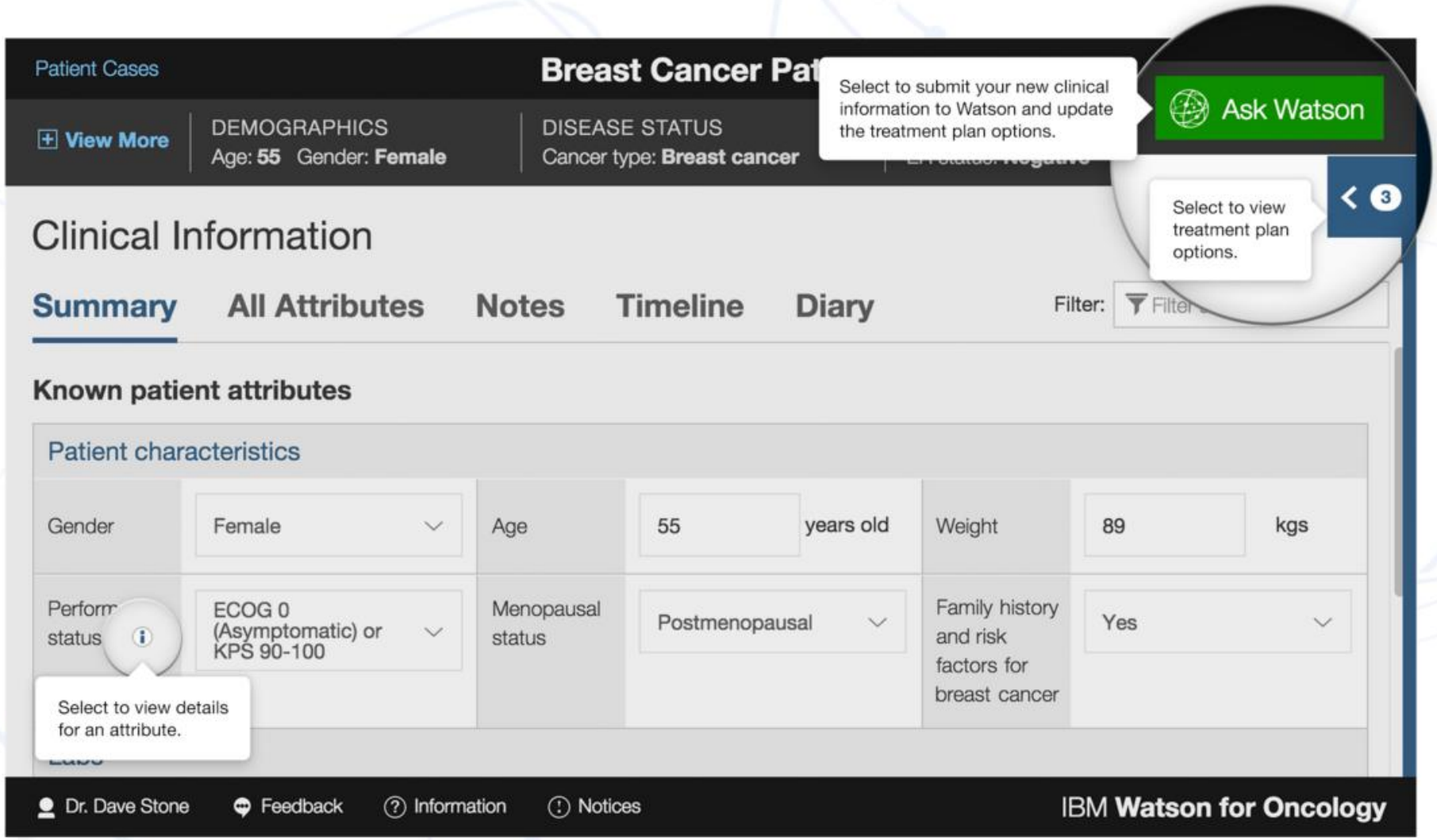
12

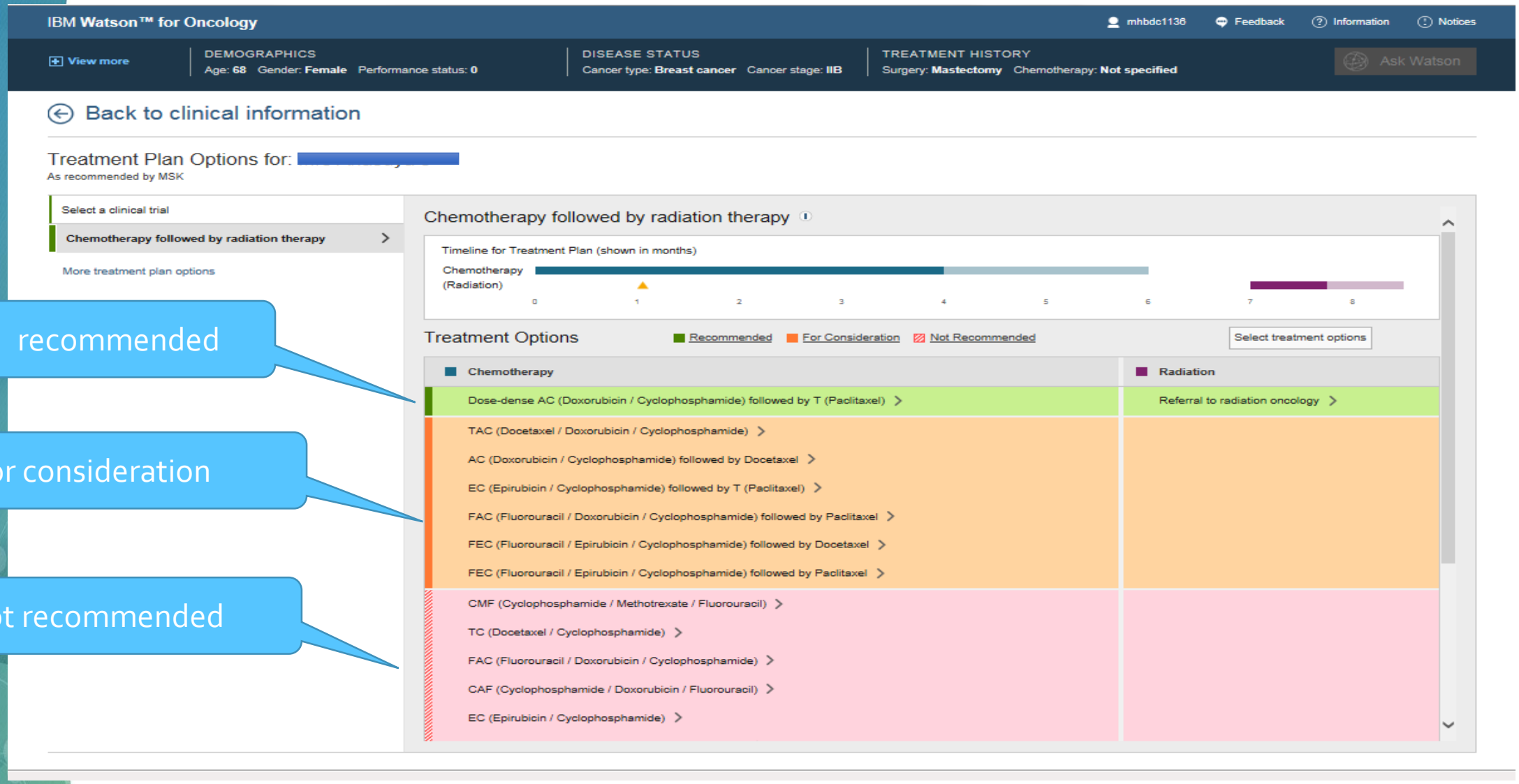
Medical journal concept annotations

IBM Watson **Natural Language Processing (NLP)**



WFO Case Attribute Summary and Help Screens





recommended

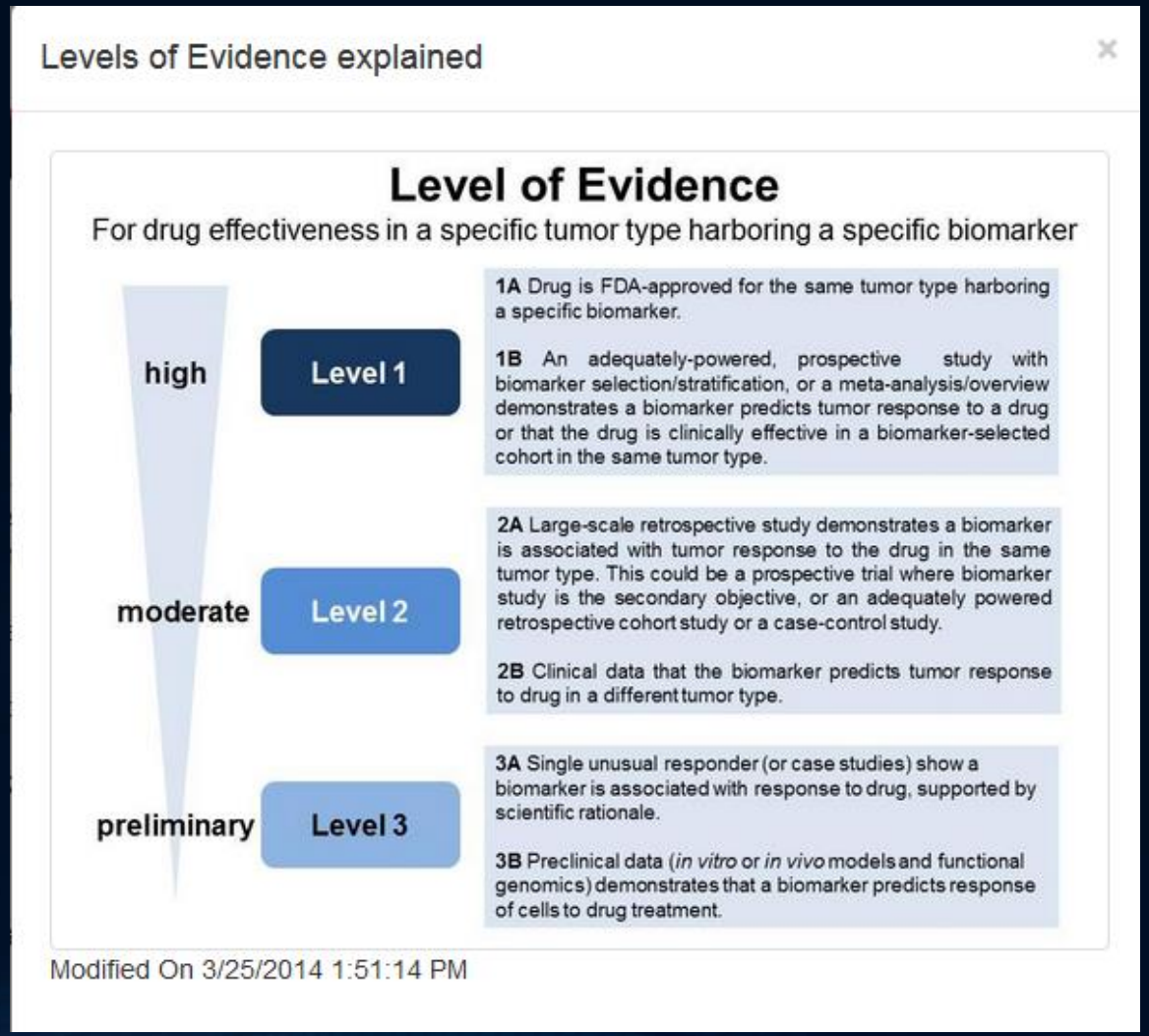
For consideration

Not recommended

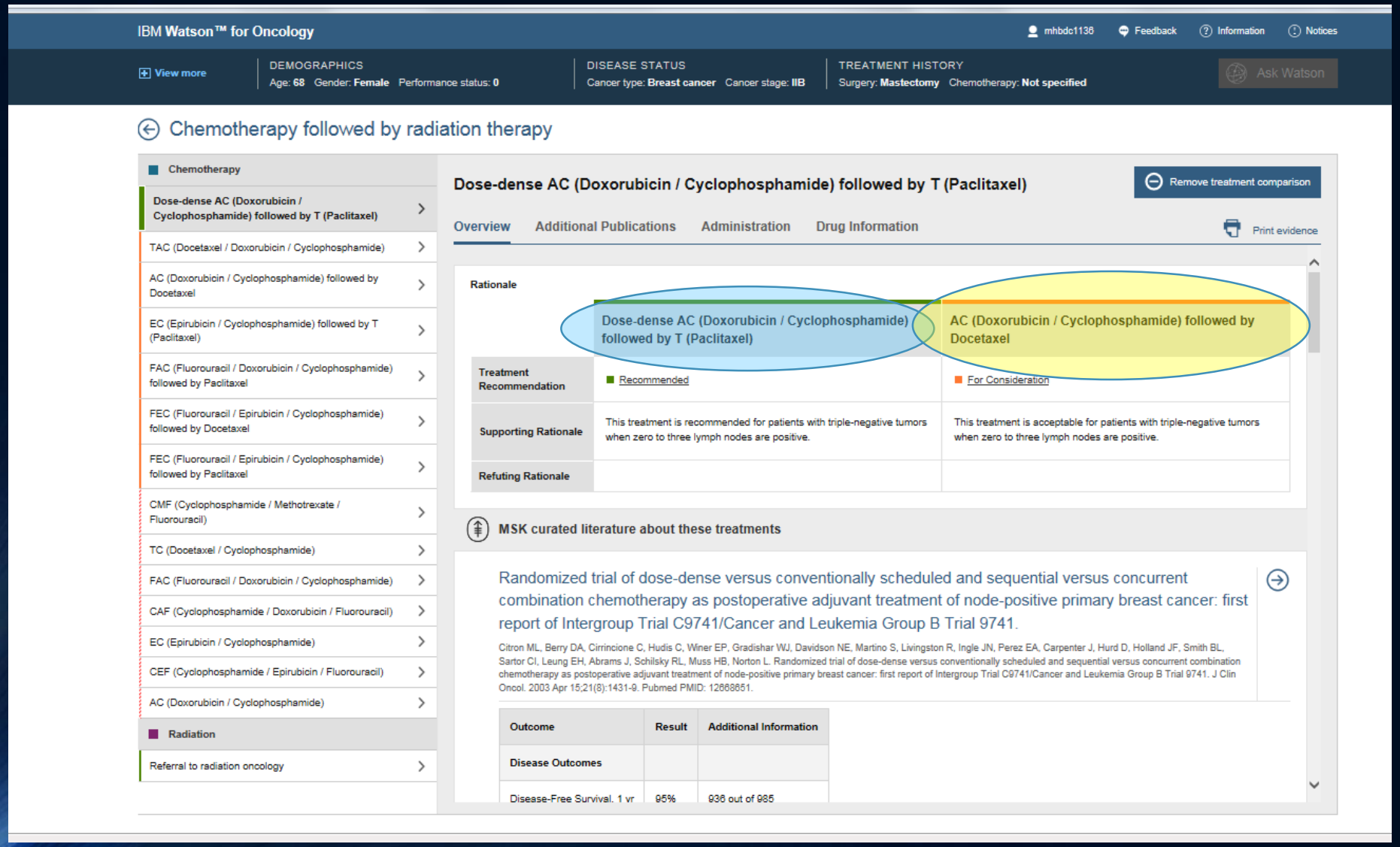
WFO Output

- Analyzes >100 patient attributes for breast cancer
- Some user attribute abstraction and WFO entry
- RX recommendations ranked in 3 color categories:
  - Green: Recommended Rx (REC)
  - Amber: For Consideration (FC)
  - Red: Not RECommended (N-REC)
- Provides supporting evidence

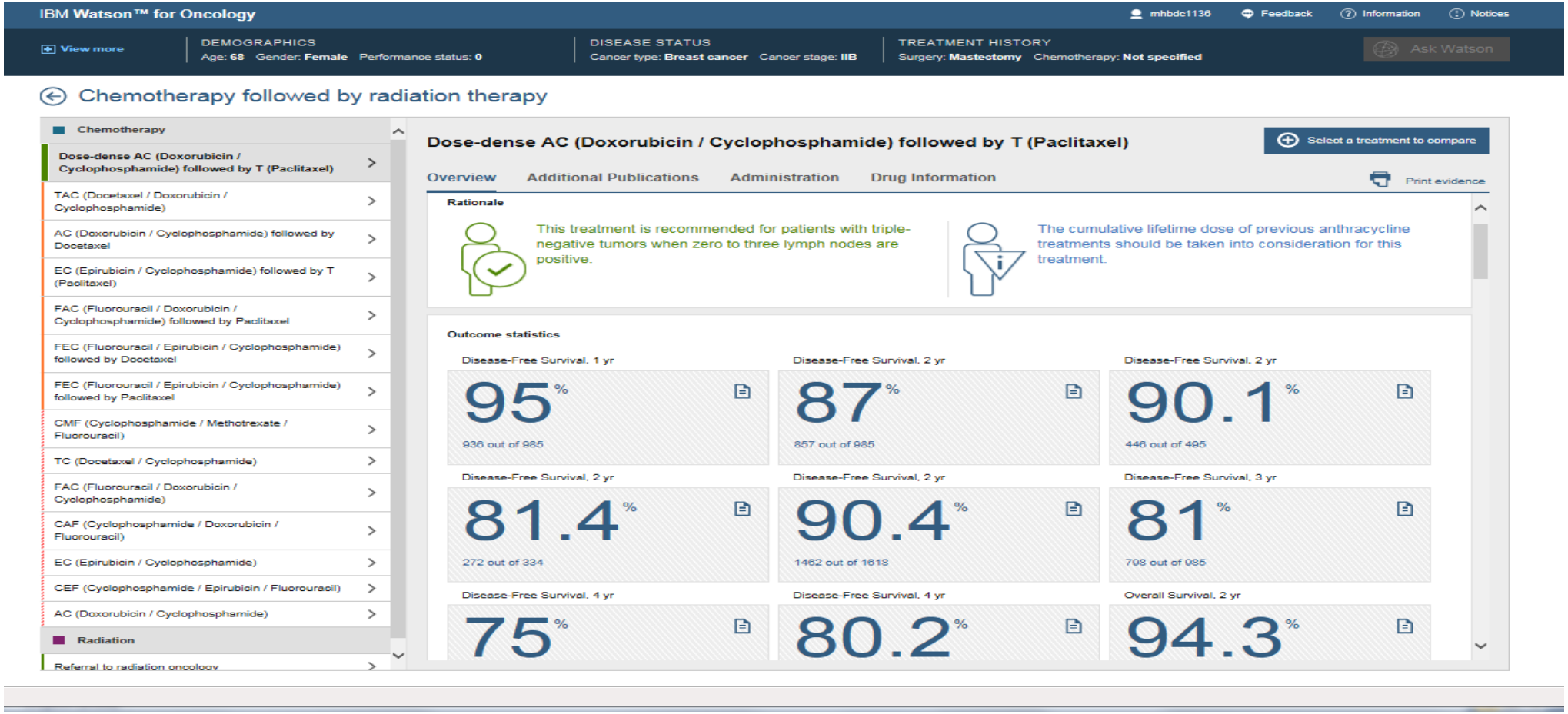
MDA Levels of Evidence Definition



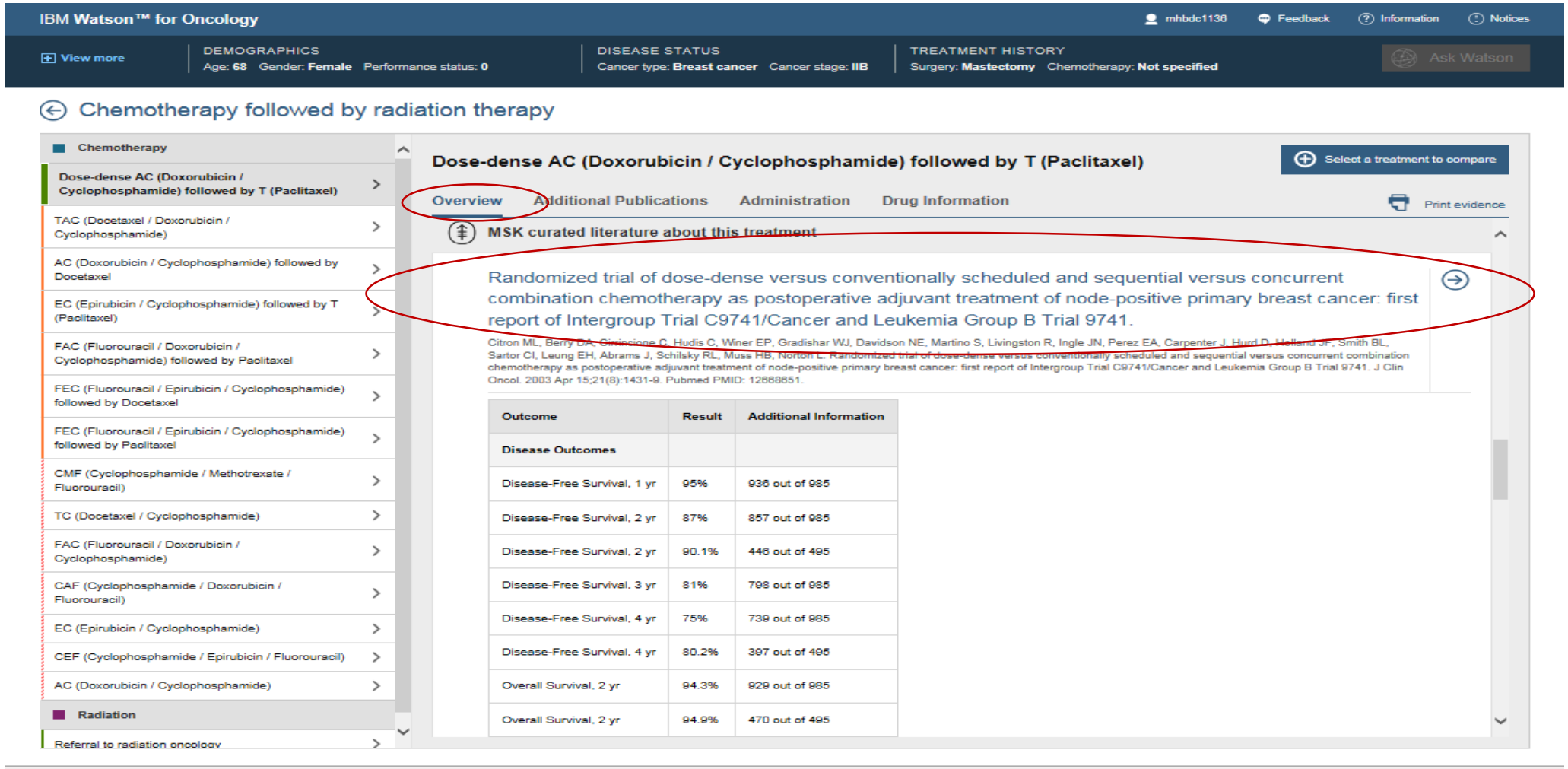
Can compare two treatment options with evidence



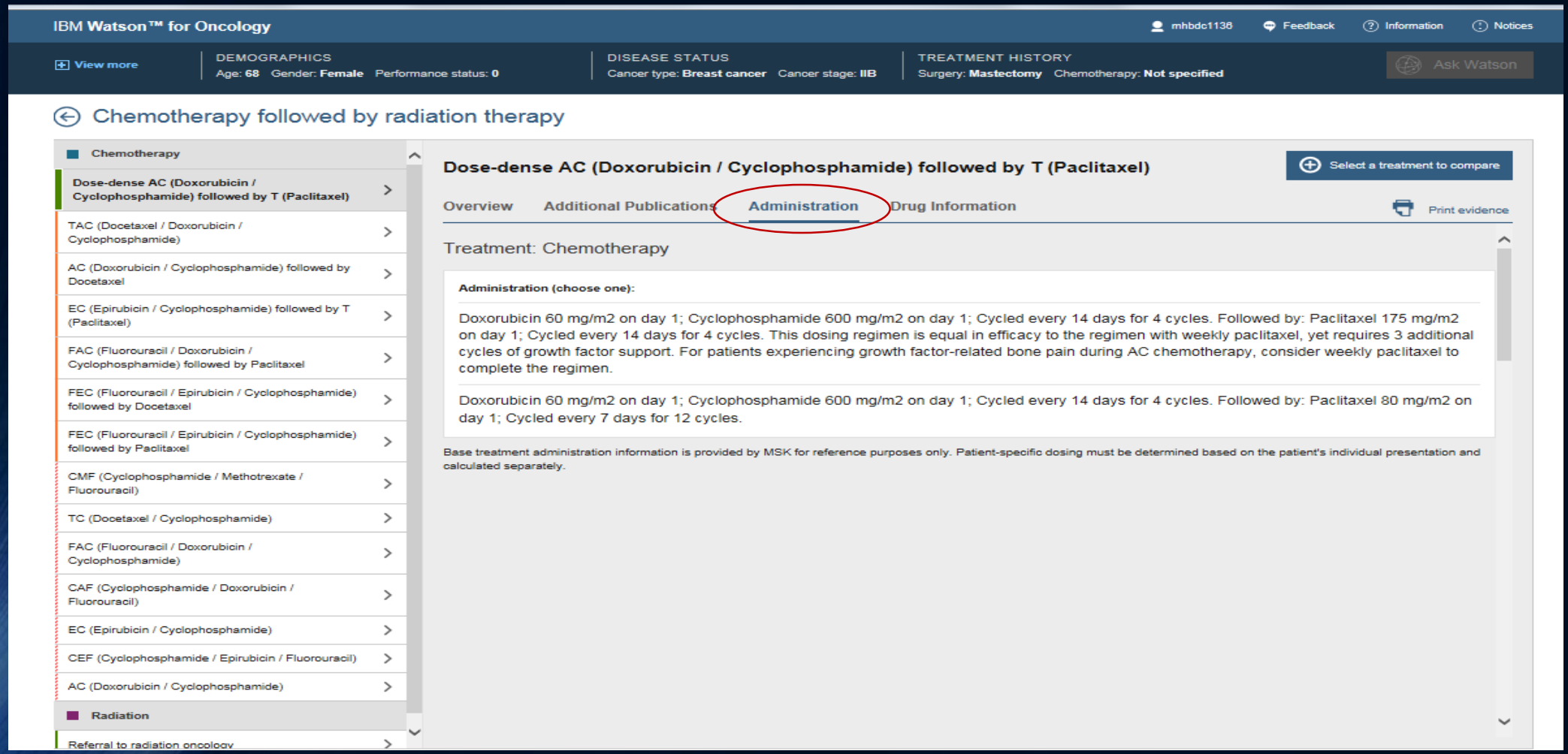
Can compare two treatment options with evidence



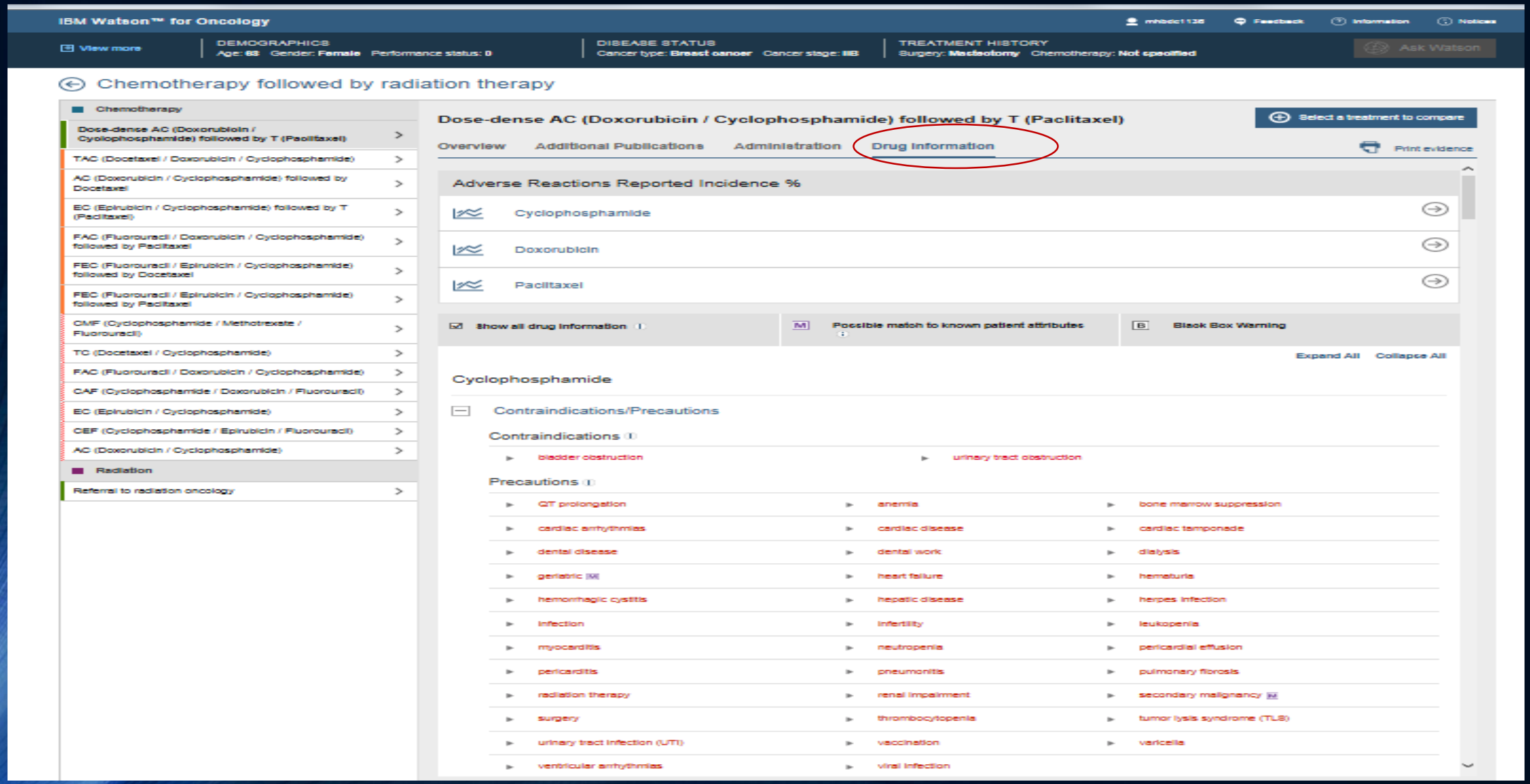
Supporting Evidence for the Recommended Treatment with Recent Trials



INFORMATION ABOUT DRUG ADMINISTRATION



DRUG INFORMATION



IBM Watson™ for Oncology

mhbdc1136 Feedback Information Notices

View more | DEMOGRAPHICS Age: 68 Gender: Fema

Ask Watson

Chemotherapy followed

Chemotherapy

- Dose-dense AC (Doxorubicin / Cyclophosphamide) followed by T (Paclitaxel)
- TAC (Docetaxel / Doxorubicin / Cyclophosphamide)
- AC (Doxorubicin / Cyclophosphamide) followed by Docetaxel
- EC (Epirubicin / Cyclophosphamide) followed by T (Paclitaxel)
- FAC (Fluorouracil / Doxorubicin / Cyclophosphamid followed by Paclitaxel
- FEC (Fluorouracil / Epirubicin / Cyclophosphamide) followed by Docetaxel
- FEC (Fluorouracil / Epirubicin / Cyclophosphamide) followed by Paclitaxel
- CMF (Cyclophosphamide / Methotrexate / Fluorouracil)
- TC (Docetaxel / Cyclophosphamide)
- FAC (Fluorouracil / Doxorubicin / Cyclophosphamide)
- CAF (Cyclophosphamide / Doxorubicin / Fluorouracil)
- EC (Epirubicin / Cyclophosphamide)
- CEF (Cyclophosphamide / Epirubicin / Fluorouracil)
- AC (Doxorubicin / Cyclophosphamide)

Radiation

- Referral to radiation oncology

Select a treatment to compare

Print evidence

Box Warning

Expand All Collapse All

Cyclophosphamide

Contraindications/Precautions

Contraindications

- bladder obstruction
- urinary tract obstruction

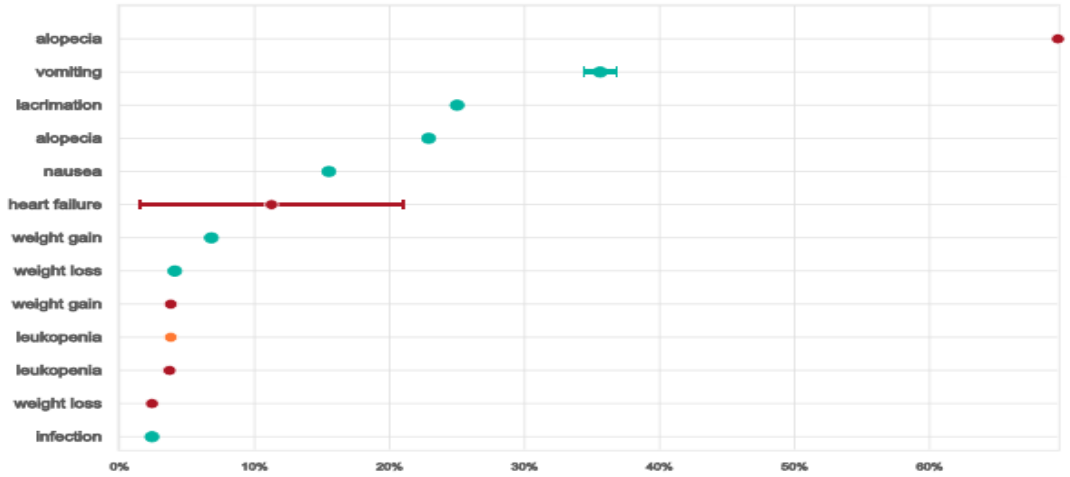
Precautions

- QT prolongation
- anemia
- bone marrow suppression

Adverse Reactions Reported Incidence % for Doxorubicin

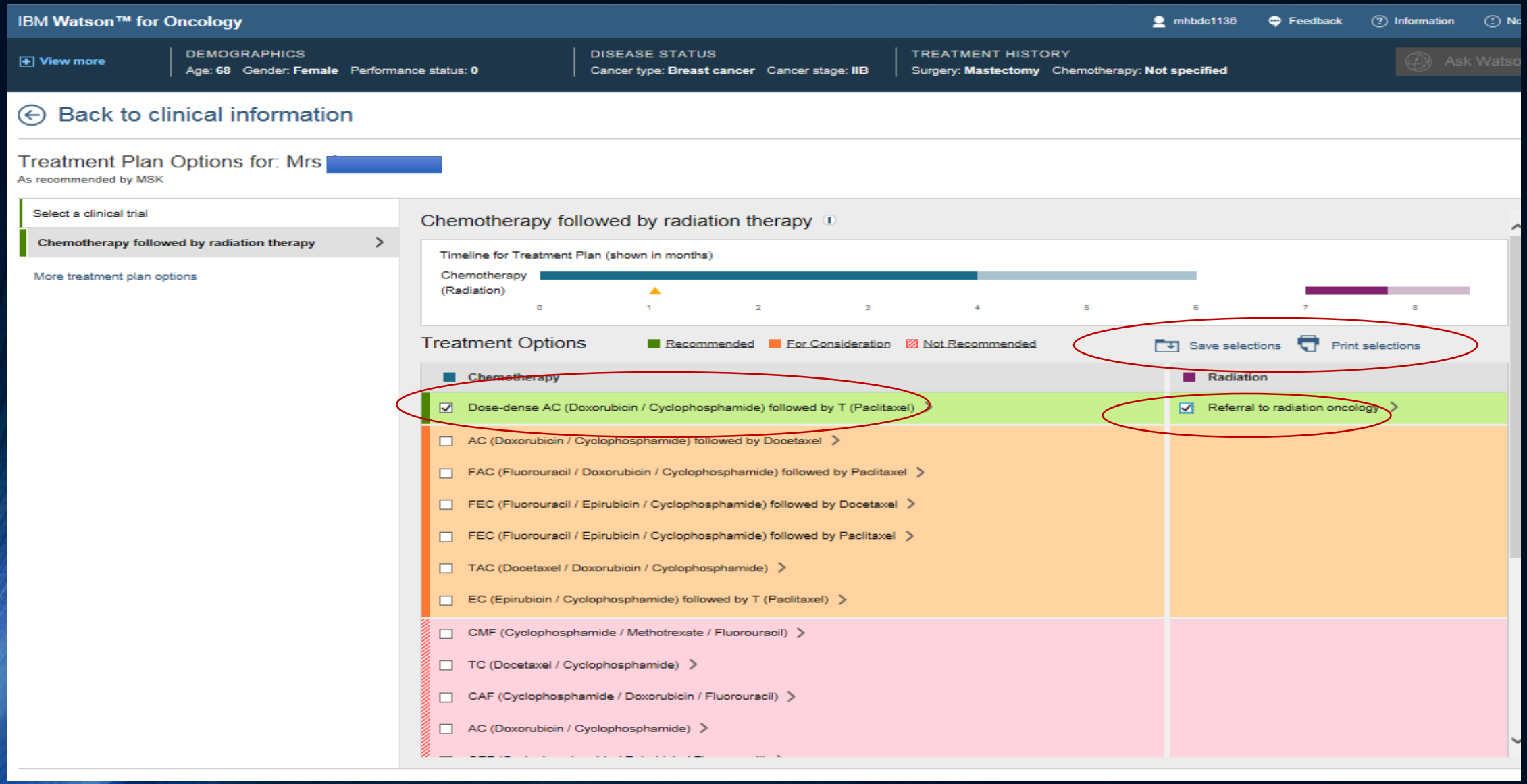
Adverse Reactions: Doxorubicin Sort by: Incidence Percentage

Severe Moderate Mild

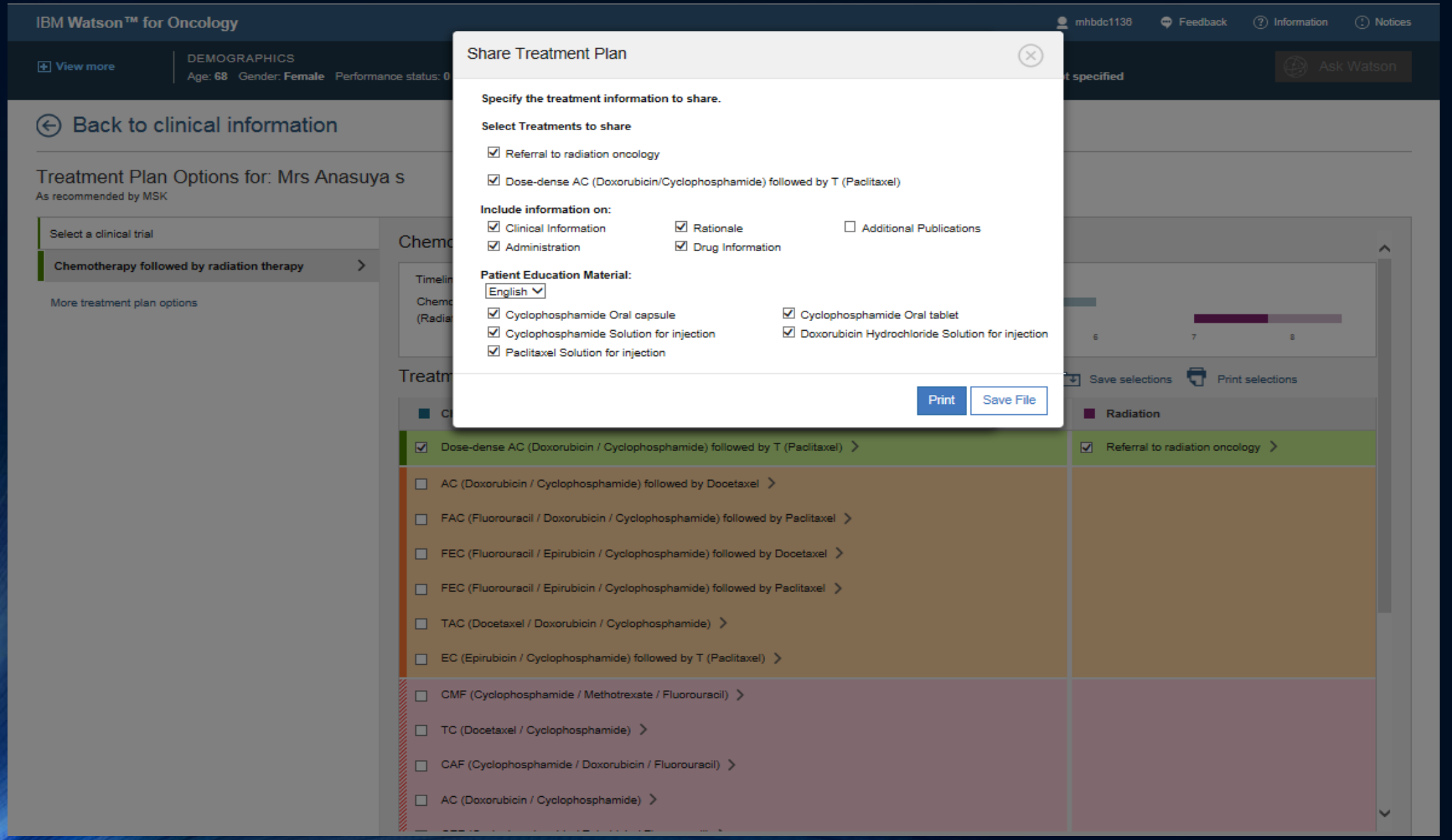


Close

SELECT TREATMENT OPTIONS AND SAVE OR PRINT



TREATMENT PLAN THAT CAN BE SHARED WITH THE PATIENT



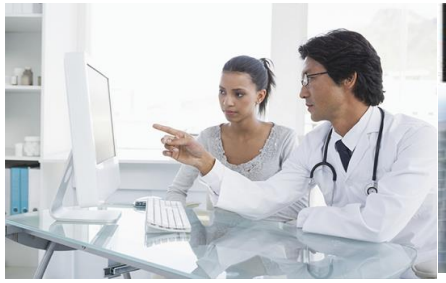
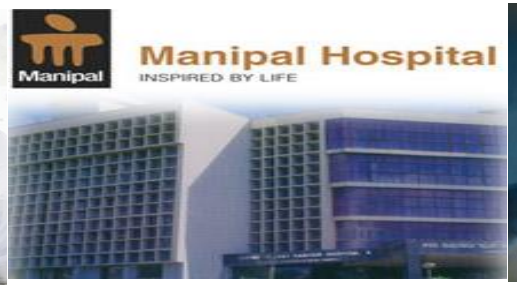
Doctors appointment list active

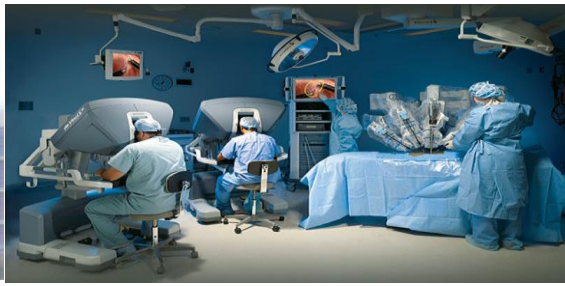
Search For Hosp No | Find | < Prev Day | Next Day > | Appt Summary | 49 New

Select	Time	Hosp No.	Name	Age	QC Status	IconProfile	Ask Watson	Consult Order	Telephone	Status	Arrive Time	Service	Remarks
☐	09:00	MHB01483384		51/Female	Electronic File		ASK WATSON	Not Ordered		Booked		Review Appointment	
☐	09:10	MHB00809334		69/Female	Electronic File		ASK WATSON	Not Ordered		Booked		Review Appointment	
☐	09:20	MHB01898624		57/Female	Electronic File		ASK WATSON	Not Ordered		Booked		Review Appointment	
☐	09:30	MHB00480408		72/Male	Electronic File		ASK WATSON	Not Ordered	3460604	Booked		Review Appointment	
☐	09:40	MHB01619563		40/Female	Electronic File		ASK WATSON	Not Ordered	26693295	Booked		Review Appointment	
☐	09:50	MHB02031574		43/Male	Electronic File		ASK WATSON	Not Ordered		Booked		Review Appointment	
☐	10:00	MHB00206261		54/Male	Electronic File		ASK WATSON	Not Ordered		Booked		Review Appointment	
☐	10:10	MHB01591905		72/Male	Electronic File		ASK WATSON	Not Ordered	23642682	Booked		Review Appointment	
☐	10:20	MHB00702910		73/Male	Electronic File		ASK WATSON	Not Ordered	26711777	Booked		Review Appointment	
☐	10:30	MHB01546086		40/Male	Electronic File		ASK WATSON	Not Ordered		Booked		Review Appointment	
☐	10:40	MHB01465207		54/Male	Electronic File		ASK WATSON	Not Ordered	9036943237	Booked		Review Appointment	
☐	10:50	MHB01861713		65/Male	Electronic File		ASK WATSON	Not Ordered	04872642230	Booked		Review Appointment	
☐	11:00	MHB01935071		6/Female	Electronic File		ASK WATSON	Not Ordered		Booked		Review Appointment	
☐	11:10	MHB02018694		68/Female	Electronic File		ASK WATSON	Not Ordered		Booked		Review Appointment	
☐	11:20	MHB00638146		74/Female	Electronic File		ASK WATSON	Not Ordered	28476115	Booked		Review Appointment	
☐	11:30	MHB01618891		53/Female	Electronic File		ASK WATSON	Not Ordered		Booked		Review Appointment	
☐	11:40	MHB01589002		66/Female	Electronic File		ASK WATSON	Not Ordered	2522694	Booked		Review Appointment	

Double-blind Concordance Study of Breast Cancer Treatment Recommendations Between Manipal Multidisciplinary Tumor Board and an Artificial Intelligence Advisor for Oncology IBM's Watson For Oncology

Manipal Comprehensive Cancer Centre
Manipal Hospital, Bangalore, India



Evaluate concordance of treatment recommendations between WFO and local expertise (Manipal Multidisciplinary Tumour Board, MMDT

Breast Cancer Concordance Study at Manipal Hospital

N = 638 cancer cases, last 3 years

T1*: Joint MMDT Best Decision

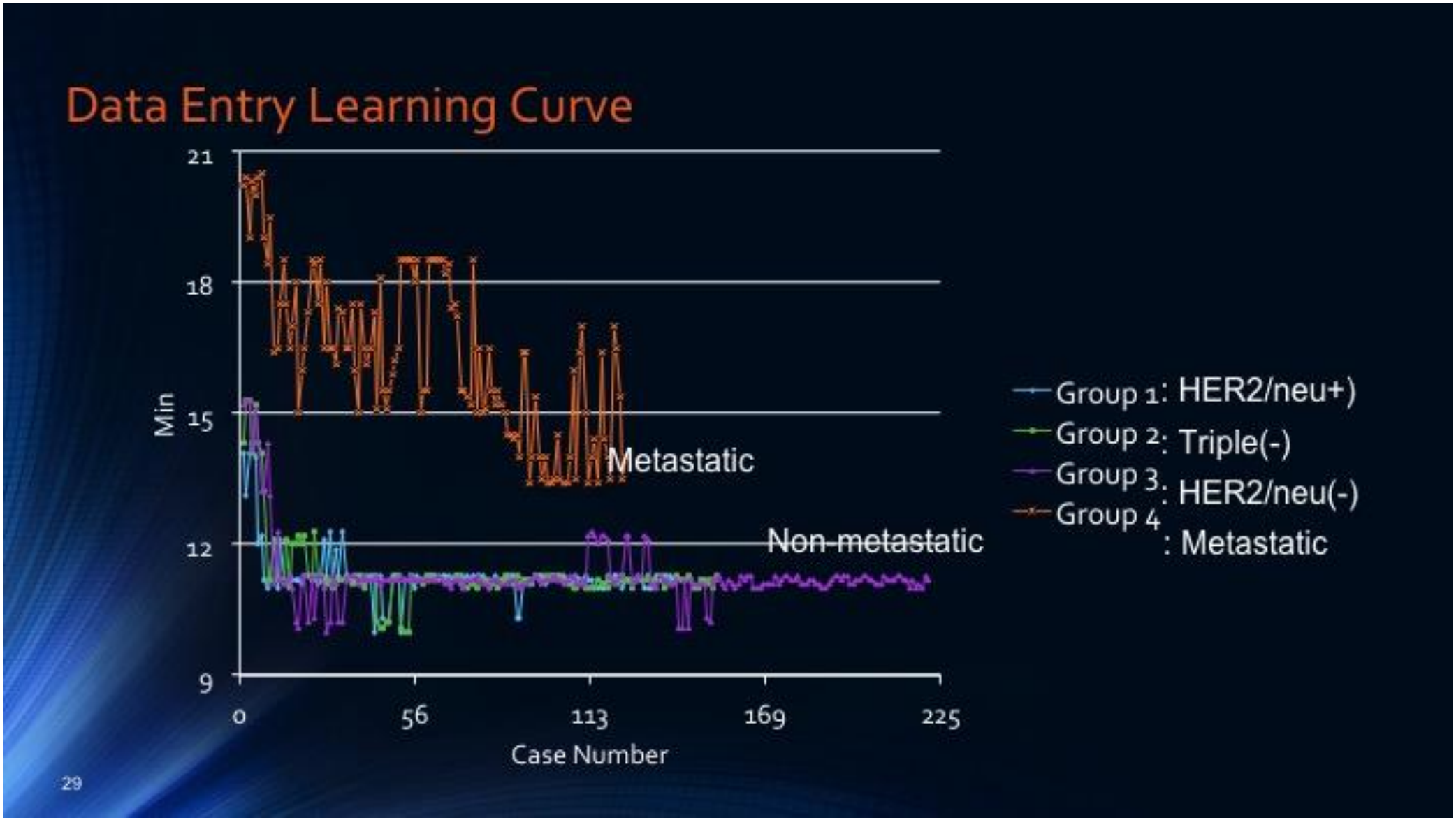
T2**: WFO Recommendation

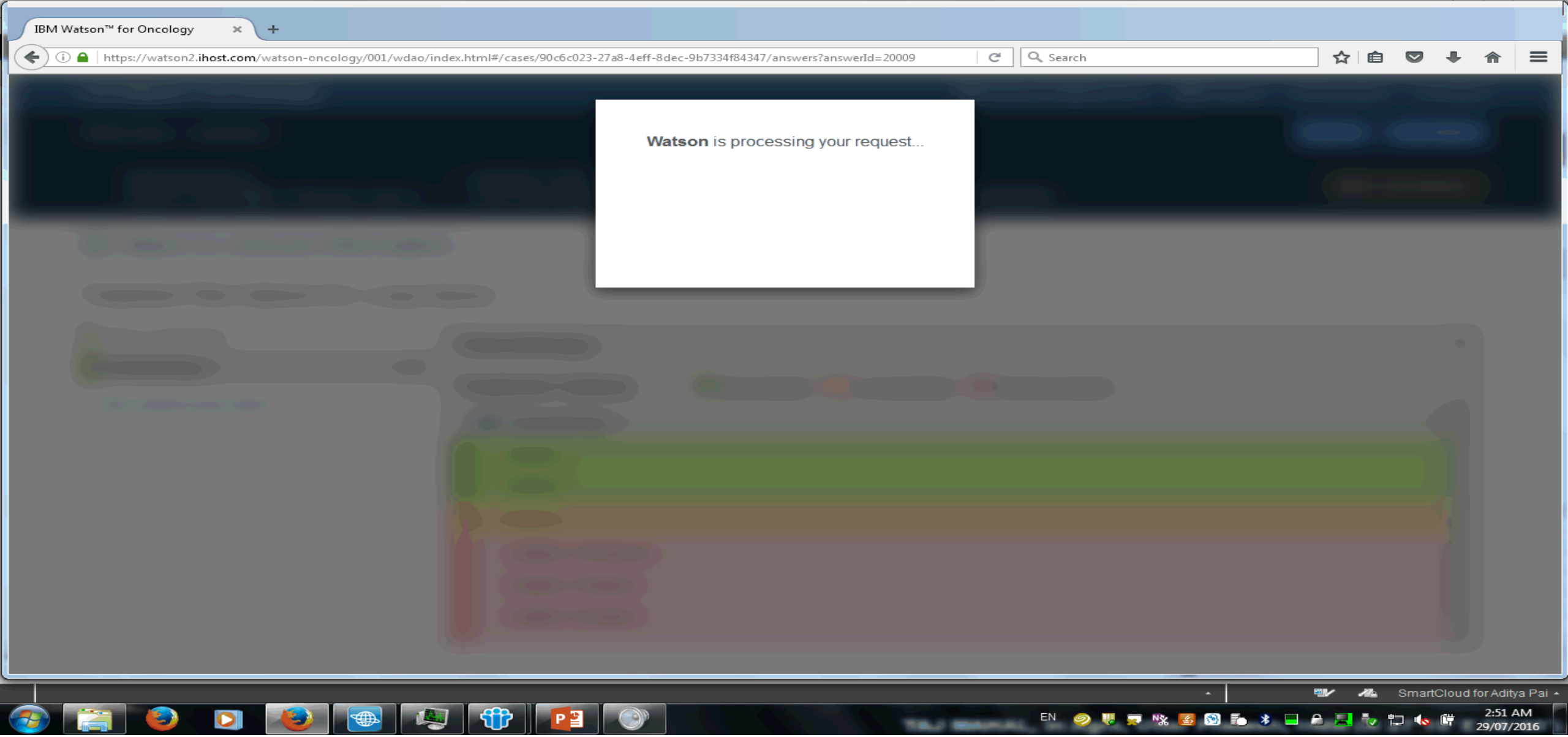
T2*: Joint MMDT Best Decision

T1–T2 Blinded Concordance

T2–T2 Blinded Concordance

* T1 Time of original treatment decision by MMDT in the past (last 1–3 years)
** T2 Time (2016) of WFO's treatment advice and of MMDT's treatment decision upon blinded re-review of non-concordant cases





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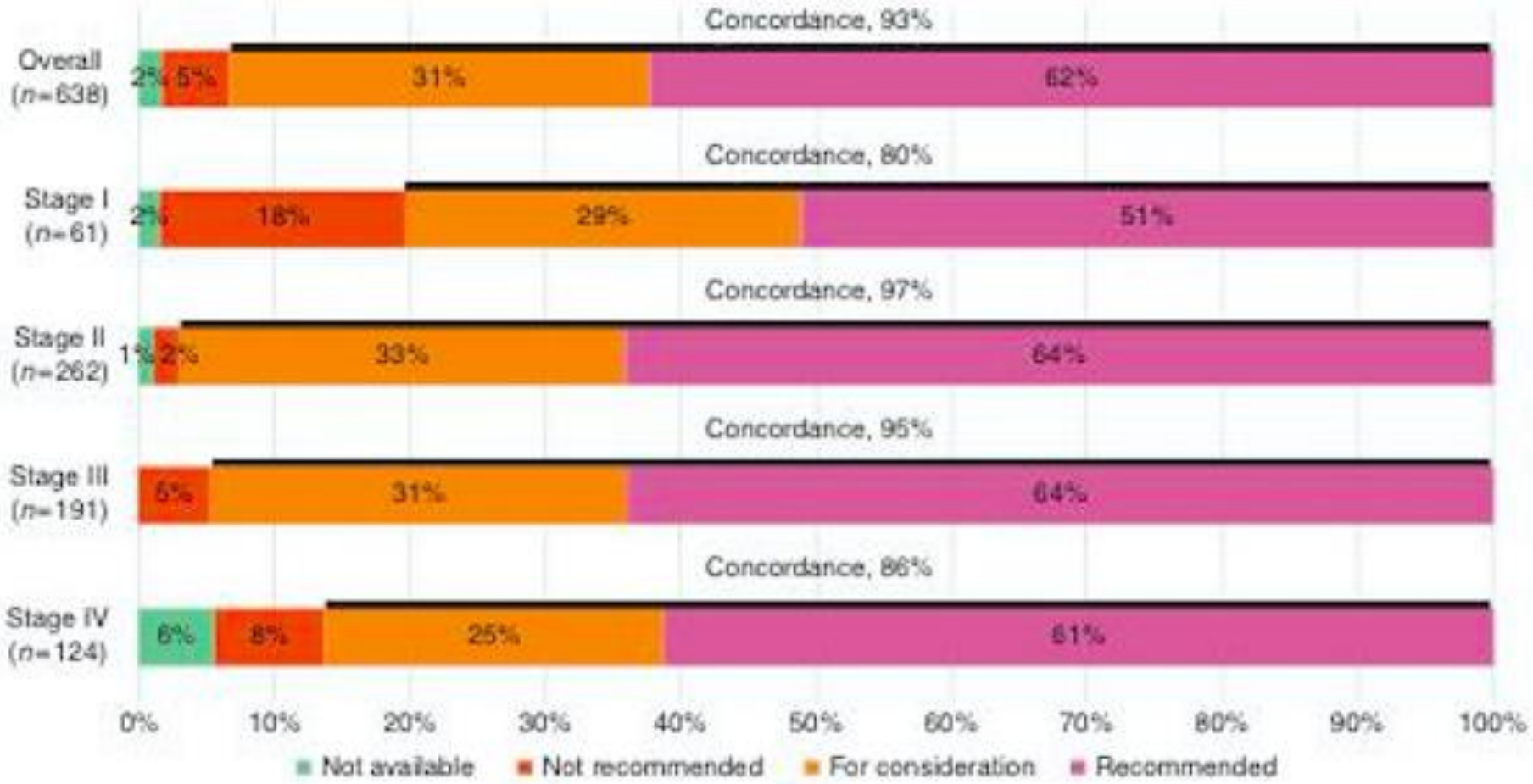


Figure 1. Treatment concordance between WFO and the MMDT overall and by stage. MMDT, Manipal multidisciplinary tumor board; WFO, Watson for Oncology.

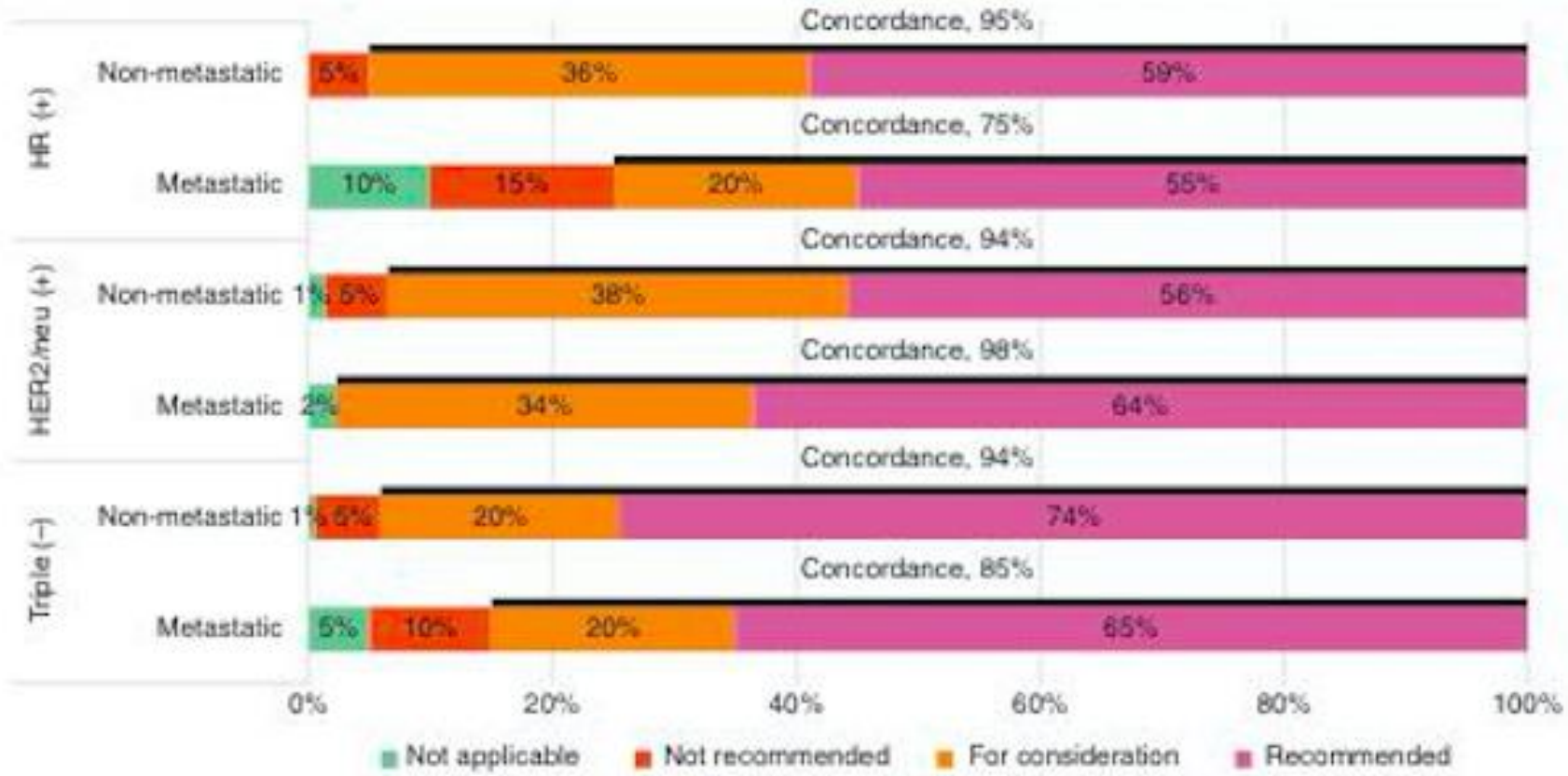
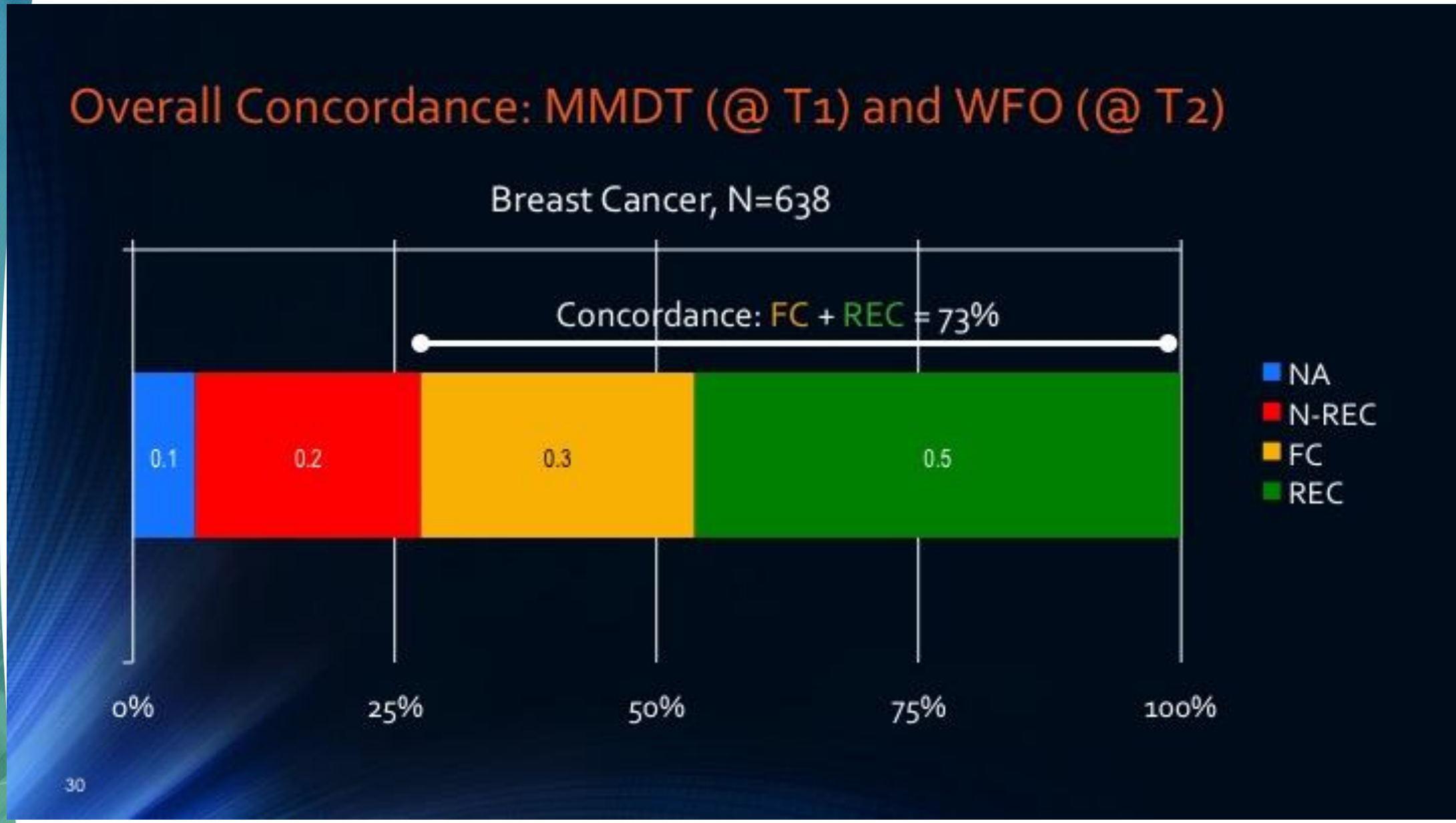
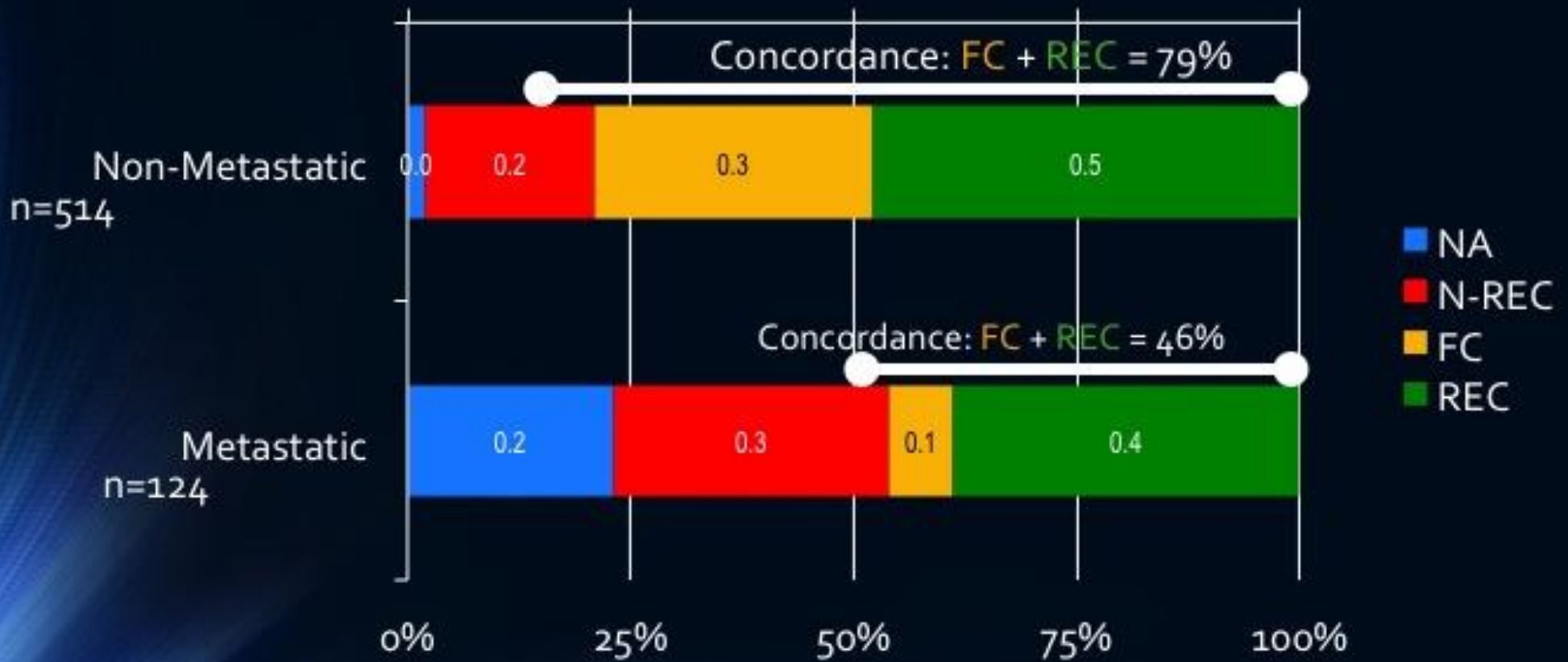


Figure 2. Treatment concordance between WFO and the MMDT by stage and receptor status. HER2/neu, human epidermal growth factor receptor 2; HR, hormone receptor; MMDT, Manipal multidisciplinary tumor board; WFO, Watson for Oncology.

Overall Concordance: MMDT (@ T1) and WFO (@ T2)



Concordance by Stage: MMDT (@T1) and WFO (@ T2)



Concordance by Receptor: MMDT (@ T1) and WFO (@ T2)

32

Concordance by Stage and Receptor: MMDT (@ T1) and WFO (@ T2)

		n	NA	N-REC	FC	REC	REC+FC
HER2/neu (+)	Non-metastatic	140	3%	13.6%	36.4%	47.1%	**83.5%**
	Metastatic	44	32%	18.2%	4.5%	45.5%	**50.0%**
HER2/neu (-)	Non-metastatic	221	0.9%	28.1%	35.7%	35.3%	**71.0%**
	Metastatic	40	28%	38%	2.5%	32.5%	**35.0%**
Triple (-)	Non-metastatic	153	2%	12%	18.3%	68.0%	**86.3%**
	Metastatic	40	10%	38%	15.0%	37.5%	**52.5%**

Concordance WFO (@T2) and MMDT (@T1* v. T2**)
(N= 638 Breast Cancer Cases)

Time Point/ Concordance	REC		REC + FC	
	n	%	n	%
T1*	296	46	463	73
T2**	381	60	574	93

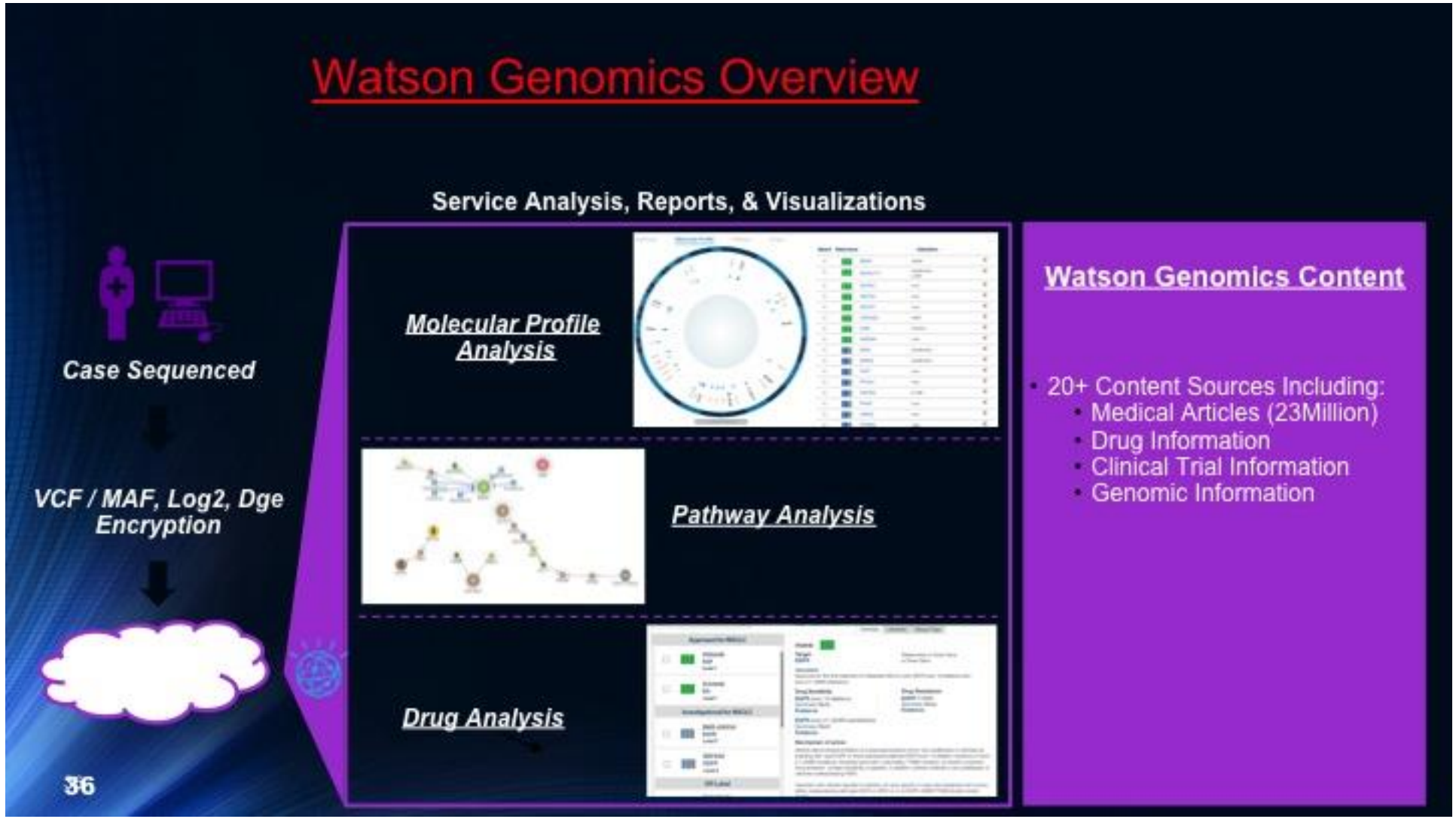
* T1 Time of original treatment decision by MMDT in the past (last 1-3 years)
** T2 Time (2016) of WFO's treatment advice and of MMDT's treatment decision upon blinded re-review of non-concordant cases

35

Re-Review of Breast Cases

Original Decision (@ T1)	Number (% Column Total)	Re-Review Decision (@T2)		Changed to	
		Not Changed (% Row Total)	Changed (% Row Total)	REC	FC
Not Available	38 (22%)	12 (32%)	26 (68%)		
Red	137 (78%)	52 (38%)	85 (62%)		
Total	175 (100%)	64 (37%)	111 (63%)	85	26

Watson Genomics Overview



Watson Genomics Overview

= Tumour

biospy

Extract DNA

(Mutated Tumour DNA)

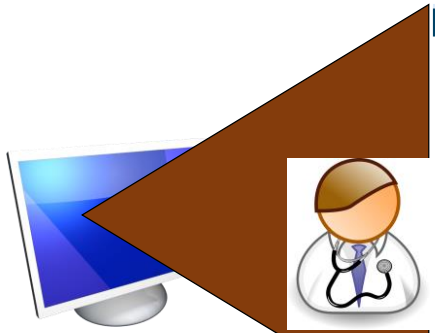
Next Generation Sequencing
- E.g. 400 gene panel

FASTQ file
(raw sequence)

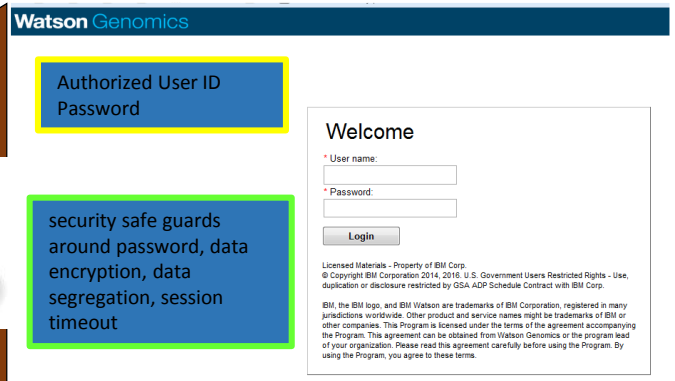
Vcf file

VCF file
Client filters out low quality reads

Within the walls of the client - **de-identification (outside WGA/IBM)**



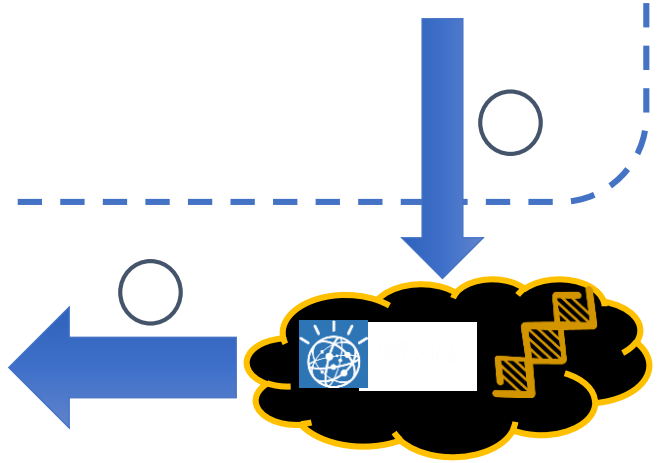
Molecular Pathologist at client



Authorized User ID
Password

security safe guards around password, data encryption, data segregation, session timeout

Molecular pathologist views analysis from Watson Genomics



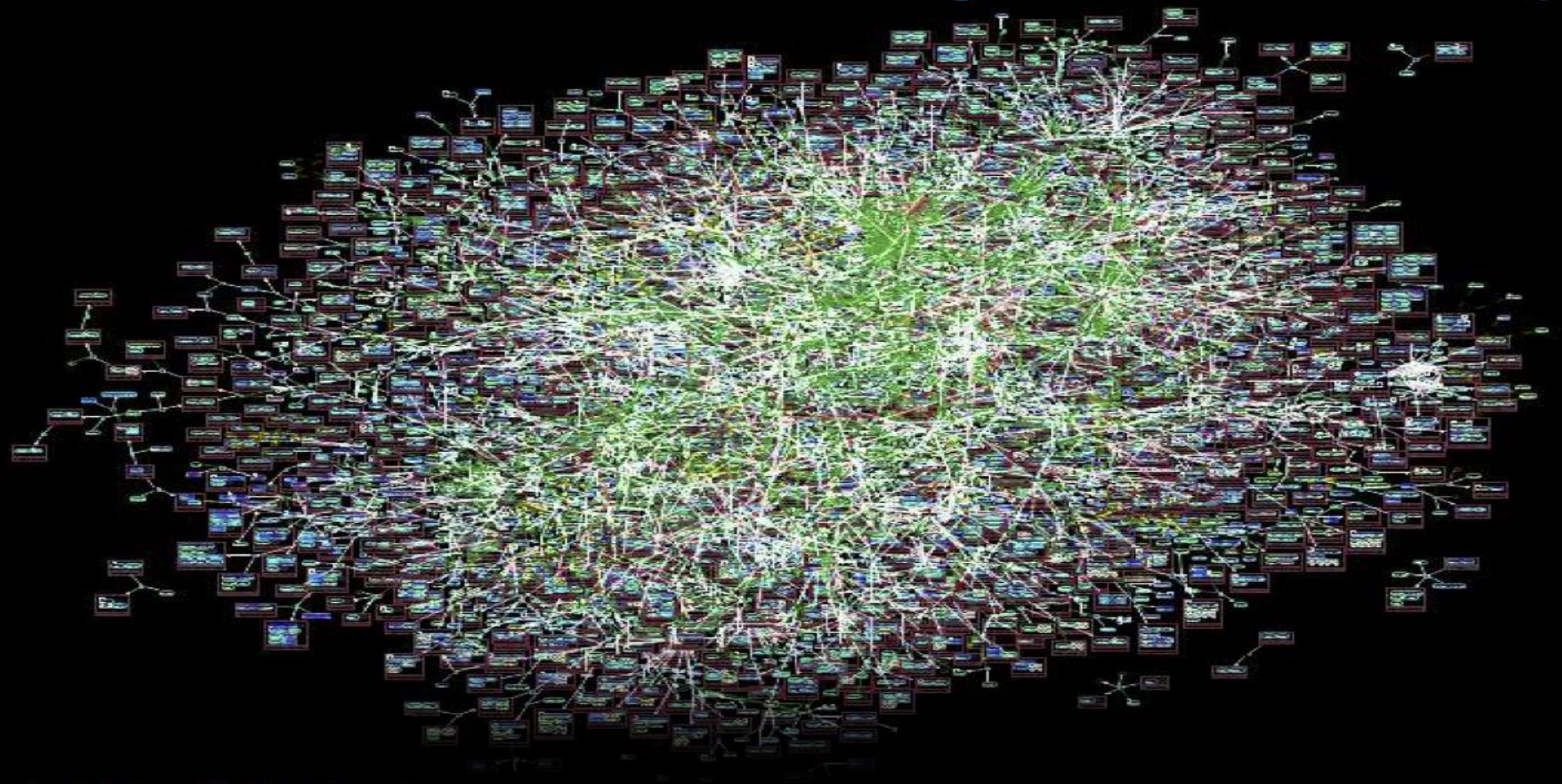
Molecular pathologist uses the analysis from WGA and "calls" the appropriate mutations and signs off on report

Medical oncologist

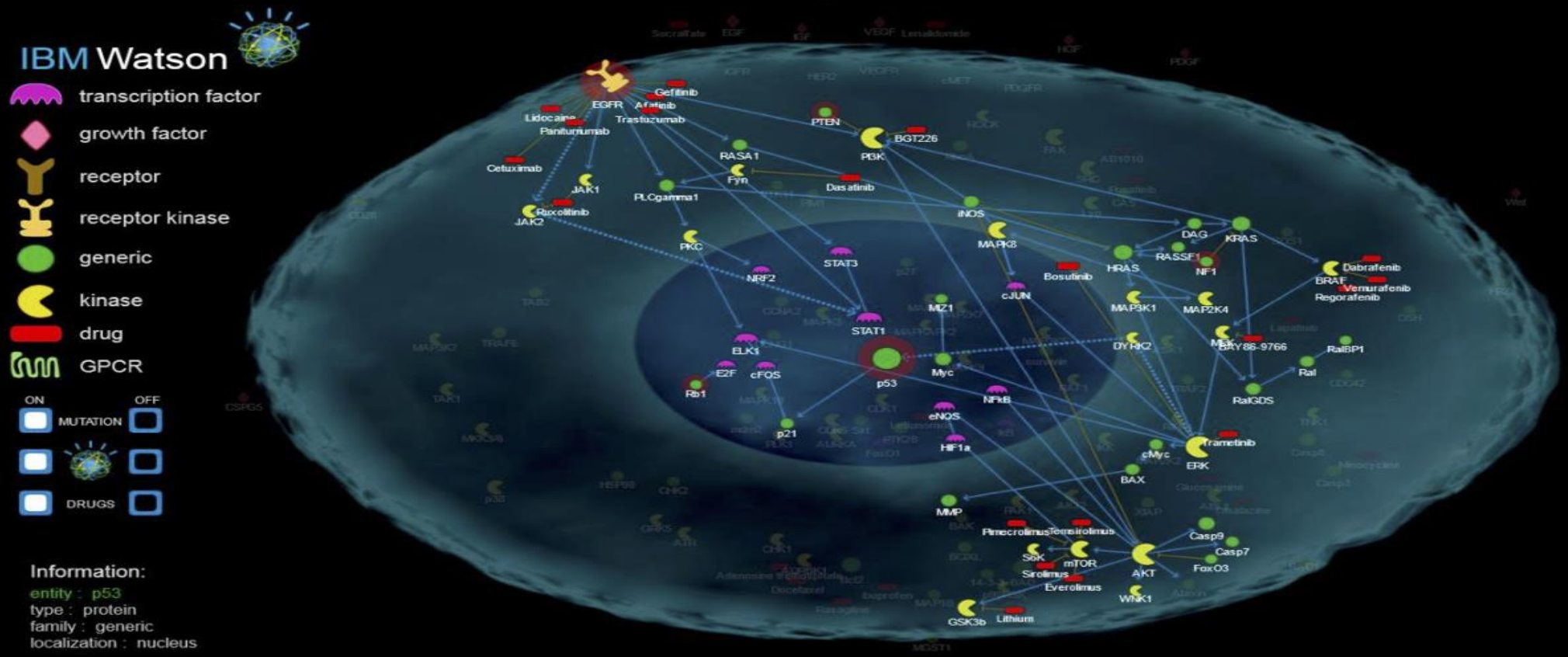
counsels

Cancer patient

What Watson Discovery Advisor is given



Watson Discovery Advisor sees



Best MDT Tumor Board equipped with Watson Oncology

“ It will be like having a capable and knowledgeable ‘colleague’ who can review the current information that relates to my patient… It is fast, thorough, and has the uncanny ability to understand how the available evidence applies to the unique individual I am treating. ”

Dr. James Miser, Bumrungrad’s Chief Medical Information Officer

What Are the Insights ?

- AI is an umbrella term, must understand whether the system is designed to
  - –act rationally (e.g. robot)
  - –think rationally (e.g. Deep Blue chess game logic)
  - –act like a human (e.g. chat–bot)
  - –think like a human think (e.g. cognitive modeling WFO)
- Value of a Clin Decision Support System determined by:
  - Content: e.g. relevant, complete, current
  - Information provided: e.g. valid, reliable, references accessible
  - Usability: e.g. comprehensible, simple, efficient, easy to use
  - Workflow integration
  - EHR integration
  - CDS–related Patient Safety
- Contemporaneous, blinded assessment of concordance is critical:
  Blinded concordance.93% when MMDT - WFO both at T2
- WFO CDS is a promising cognitive computing tool that warrants further evaluation in a variety of
  clinical settings and a variety of study designs.
- AI CDS systems require transparency about evidence validating the quality of its components, safety,
  usability and work flow integration

What Are the Insights ?

- This study examined concordance only
- Not designed to evaluate why differences in recommendations occurred, inferiority/superiority of recommendations, impact of WFO on workflow, etc.
- Important to assess blinded concordance between local experts and WFO at the same point in time:
  Blinded concordance 73% when MMDT@T1- WFO @T2 vs 93% when MMDT–WFO both at T2.
- WFO may reduce the cognitive burden on oncologists by providing clinically actionable insights to assist in treating patients.
- WFO is a promising cognitive computing tool that warrants further evaluation in a variety of clinical settings and a variety of study designs.
- The role of WFO will always be consultative; WFO cannot replace human clinical judgment and the essential patient-doctor relationship

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ORIGINAL ARTICLE

Watson for Oncology and breast cancer treatment recommendations: agreement with an expert multidisciplinary tumor board

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Background: Breast cancer oncologists are challenged to personalize care with rapidly changing scientific evidence, drug approvals, and treatment guidelines. Artificial intelligence (AI) clinical decision-support systems (CDSSs) have the potential to help address this challenge. We report here the results of examining the level of agreement (concordance) between treatment recommendations made by the AI CDSS Watson for Oncology (WFO) and a multidisciplinary tumor board for breast cancer.

Patients and methods: Treatment recommendations were provided for 638 breast cancers between 2014 and 2016 at the Manipal Comprehensive Cancer Center, Bengaluru, India. WFO provided treatment recommendations for the identical cases in 2016. A blinded second review was carried out by the center's tumor board in 2016 for all cases in which there was not agreement, to account for treatments and guidelines not available before 2016. Treatment recommendations were considered concordant if the tumor board recommendations were designated 'recommended' or 'for consideration' by WFO.

Results: Treatment concordance between WFO and the multidisciplinary tumor board occurred in 93% of breast cancer cases. Subgroup analysis found that patients with stage I or IV disease were less likely to be concordant than patients with stage II or III disease. Increasing age was found to have a major impact on concordance. Concordance declined significantly ($P \leq 0.02$; $P < 0.001$) in all age groups compared with patients <45 years of age, except for the age group 55–64 years. Receptor status was not found to affect concordance.

Conclusion: Treatment recommendations made by WFO and the tumor board were highly concordant for breast cancer cases examined. Breast cancer stage and patient age had significant influence on concordance, while receptor status alone did not. This study demonstrates that the AI clinical decision-support system WFO may be a helpful tool for breast cancer treatment decision making, especially at centers where expert breast cancer resources are limited.

Key words: Watson for Oncology, artificial intelligence, cognitive clinical decision-support systems, breast cancer, concordance, multidisciplinary tumor board

Introduction

Oncologists who treat breast cancer are challenged by a large and rapidly expanding knowledge base [1, 2]. As of October 2017, for example, there were 69 FDA-approved drugs for the treatment of breast cancer, not including combination treatment regimens [3]. The growth of massive genetic and clinical databases, along with computing systems to exploit them, will accelerate the speed of breast cancer treatment advances and shorten the cycle time for changes to breast cancer treatment guidelines [4, 5]. In addition, these information management challenges in cancer care are occurring in a practice environment where there is little time available for tracking and accessing relevant information at the point of care [6]. For example, a study that surveyed 1117 oncologists reported that on average 4.6 h per week were spent keeping

...mendations after the initial and blinded second reviews

...ases (*N* = 638)	Concordant cases, *n* (%)			Non-concordant cases, *n* (%)		
	Recommended	For consideration	Total	Not recommended	Not available	Total
Initial review ($T1_{MMDT}$ versus $T2_{WFO}$)	296 (46)	167 (26)	463 (73)	137 (21)	38 (6)	175 (27)
Second review ($T2_{MMDT}$ versus $T2_{WFO}$)	397 (62)	194 (30)	591 (93)	36 (5)	11 (2)	47 (7)

$T1_{MMDT}$, original MMDT recommendation from 2014 to 2016; $T2_{WFO}$, WFO advisor treatment recommendation in 2016; $T2_{MMDT}$, MMDT treatment recommendation in 2016; MMDT, Manipal multidisciplinary tumor board; WFO, Watson for Oncology.

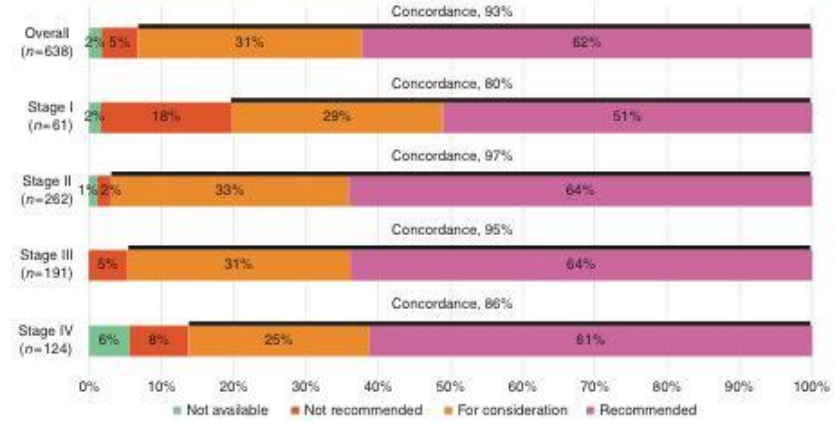

Figure 1. Treatment concordance between WFO and the MMDT overall and by stage. MMDT, Manipal multidisciplinary tumor board; WFO, Watson for Oncology.

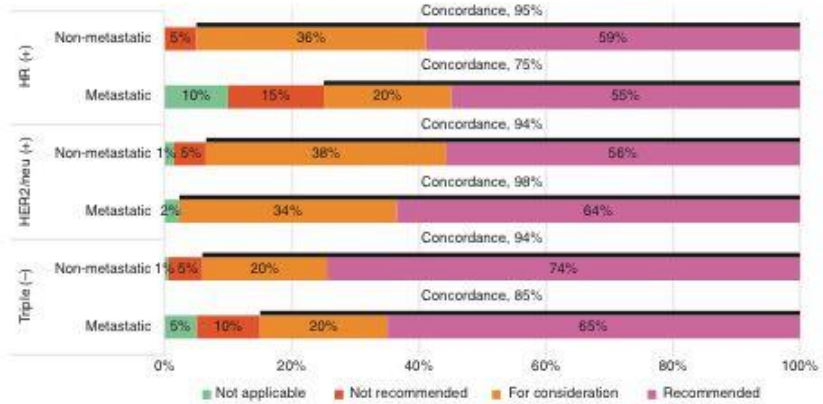

Figure 2. Treatment concordance between WFO and the MMDT by stage and receptor status. HER2/neu, human epidermal growth factor receptor 2; HR, hormone receptor; MMDT, Manipal multidisciplinary tumor board; WFO, Watson for Oncology.

Thanks