City of Hope®

Annual

Advances and Innovations in Endoscopic Oncology and Multidisciplinary Gastrointestinal Cancer Care

Getting into the NCCN Guidelines: What is Needed and How?



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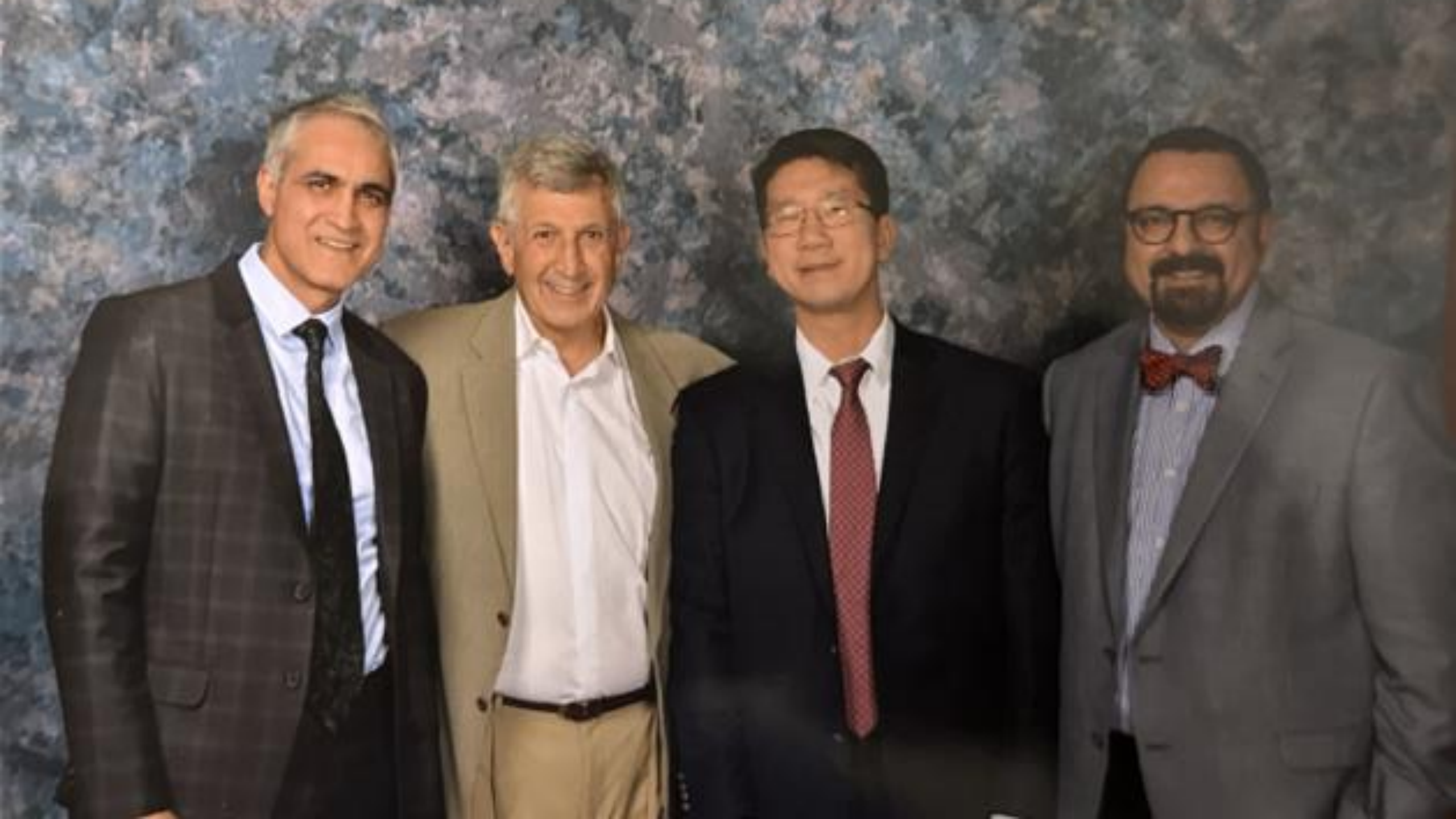
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Disclosures

- I do not have any financial disclosures
- I am a member of a NCCN panel
- Information discussed is publicly available

This presentation and/or comments will provide a balanced, non-promotional, and evidence-based approach to all diagnostic, therapeutic and/or research related content.



Agenda

- **The basics** — What, Who, Why?
- **How to propose a change?**
- **How evidence is evaluated**?
- **Case study**

What Are the NCCN Guidelines?



- Evidence-based, consensus-driven
- 88 disease- and topic-specific guidelines, built and maintained by 64 multidisciplinary panels
- Category of Evidence and Consensus
- Reviewed at least once a year, with interim updates

Why Does Mention in the Guidelines Matter?

- NCCN Category status drives payer coverage
  - CMS and most private insurers use it to decide what they will reimburse
- Inclusion (or exclusion) how a new technique reaches routine practice
- Interventional, surgical, and endoscopic procedures are proposed and voted on
  - Driven by evidence
  - Not always possible with procedural therapies
  - Need for active members on the panel

NCCN Categories of Preference



- Evidence and Consensus grades (1, 2A, 2B, 3) say how well-supported a recommendation is. Categories of Preference say which option the Panel would pick first — a separate, complementary layer
- **Preferred:** based on superior efficacy, safety, and evidence
- **Other recommended:** somewhat less efficacious or more toxic, based on less mature data, or treatment options for similar outcomes
- **Useful in certain circumstances:** appropriate for selected patient populations, defined with the recommendation

Who Develops the Guidelines?



- 34 NCCN Member Institutions nominate a Steering Committee, which oversees process and appoints Panel members
- Each disease/topic Panel has 28–35 volunteer multidisciplinary “experts”
  - Includes surgeons, interventional radiologists, and gastroenterologists where relevant
- An NCCN Guidelines Team of staff scientists, editors and patient advocates supports the Panel and drafts the algorithms
- No industry funding is accepted for guideline development — a strict bylaws attempt to prevent COI

The Annual Update Cycle



- Literature review
  - NCCN staff search literature and key meeting abstracts since the last update
- Institutional Review
  - Clinicians at Member Institutions flag data that should change practice
- External submissions
  - Clinicians, societies, and industry request changes through the public portal
- Panel meeting
  - All requests are discussed and voted on
  - Interim versions can follow for FDA approvals or urgent new evidence

Two Paths to Propose a Change

Institutional Review

- Internal
  - Driven by clinical experts at NCCN Member Institutions
- Identifies where new data has changed the standard of care
- Feeds the annual update

External Submission

- Open
  - Clinicians, professional societies, patient advocates, and industry can all apply
- Submitted online with supporting peer-reviewed evidence
- This is the route most procedures are entered

How an External Submission Works

1

Submit

File a request through the online Submission Portal before the Panel meeting, with peer-reviewed evidence attached

2

Panel Reviews & Votes

Materials provided to Panel leadership and members in advance; the request is discussed and voted on by disease panel

3

Decision Published

Publicly available

What Counts as Strong Procedural Evidence?

Why Procedures Are Different

- Blinding is near impossible
- Outcomes depend on operator learning curve and volume, not just the technique itself
- Equipoise is hard once a technique already taken off

How the Field Adapts

- RCTs specifically for procedures
- Large registries and cohort studies
- Result: procedures more often land at Category 2A than Category 1 — strong consensus, without a phase 3 trial
- Specialty society adoption

Evidence & Consensus Categories

Every recommendation is graded for evidence quality and panel agreement. Category 1 and 2A both require ≥85% panel support — the difference is the strength of the underlying data

Cat 1

High evidence, ≥85% consensus

Cat 2A

Lower evidence, ≥85% consensus

Cat 2B

Lower evidence, 50–84% consensus

Cat 3

Any evidence, major disagreement

87%

of recommendations are Cat 2A

~0%

of recommendations are Cat 3

Case Study: ESD

- Origin (1990s, Japan) — endoscopists develop ESD to remove early gastric cancers sparing gastrectomy
- Evidence builds (2000s–2020) — Japanese cohorts define “absolute” and “expanded” indications; JCOG1009/1010
- Societies formalize it (2021–2023) — JGES/JGCA, ESGE, and ASGE publish GRADE-reviewed ESD guidelines
- NCCN adopts it — the Panel cites ASGE (2023) and ESGE (2022), listing ESD/EMR for selected T1a tumors
- A single-country technique became guideline-listed via the evidence → specialty society guideline → NCCN



The Same Pathway, Two More Specialties

Surgery: MIS Gastrectomy

- Laparoscopic gastrectomy spread through Asia in the 1990s for early-stage disease
- Japan, Korea, and China each ran national phase 3 RCTs (JCOG, KLASS-01/02, CLASS-01) proving noninferiority to open surgery
- Laparoscopic/robotic gastrectomy as an option for experienced surgeons

IR: Y-90 Radioembolization

- FDA-approved as a device (2002) for unresectable HCC, then built out with cohort data and one phase 2 RCT vs. chemoembolization
- Registries, not a phase 3 trial, carried most of the evidence weight
- Society endorsement
- NCCN's Hepatobiliary Cancers guideline lists it as locoregional therapy for select unresectable disease





Case Study: Heated Intraperitoneal Chemotherapy (HIPEC)

- Cytoreductive surgery (CRS) removes all visible tumor from the peritoneal surface; HIPEC bathes the abdomen in heated chemotherapy right after, to kill what's left behind
- It is one procedure, but NCCN treats it differently in every guideline where it appears, because the evidence behind it is different each time
- Appendiceal cancer — cohort data made it the standard of care for peritoneal disease
- Ovarian cancer — a positive phase 3 trial earned HIPEC a place in the algorithm
- Colon cancer — a negative phase 3 trial pulled it back to a highly selective option

Appendiceal Cancer: CRS-HIPEC as the Standard

- Appendiceal tumors spread almost exclusively across the peritoneal surface, rarely to distant organs — a biology well suited to regional surgery
- No phase 3 trial exists — the disease is too rare to randomize — so the evidence is retrospective cohorts
- Multiple Societies (SSO, PSOGI, ESSO, Chicago Consensus) despite the lack of a trial
- NCCN adopts it —
  - CRS-HIPEC the treatment of choice for low-grade disease (2025)
- When a disease is rare enough, strong consensus can substitute for a randomized trial



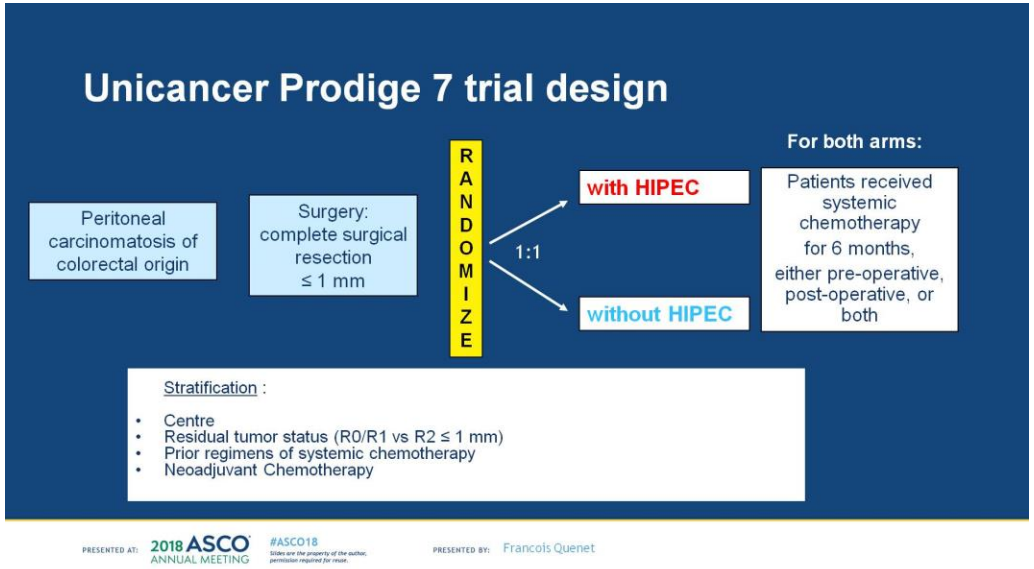
Ovarian Cancer: CRS-HIPEC After a Positive Trial

- Neoadjuvant Chemotherapy and CRS standard for for stage III ovarian cancer
- OVHIPEC-1 (van Driel et al, NEJM 2018) randomized 245 patients to surgery alone vs. surgery plus HIPEC
- HIPEC significantly improved recurrence-free and overall survival, with no added rate of serious complications
- NCCN adopts it — the Ovarian Cancer Panel lists HIPEC at interval cytoreductive surgery as an option, citing OVHIPEC-1 directly
- Controversy still exists



Colon Cancer: Reversal of fortune

- Cohort data through the 2000s led many centers to pair HIPEC with CRS for colorectal peritoneal metastases – NCCN guidelines recommended at expert centers
- PRODIGE 7 (Quénet et al, Lancet Oncol 2021) randomized 265 patients to CRS alone vs. CRS plus oxaliplatin HIPEC
- No overall survival benefit from adding HIPEC — and more major complications in the HIPEC arm
- NCCN's response — CRS remains recommended; HIPEC itself is now a conditional option for a narrow, selected subset only
  - Insurance denials as a result



COI

- No industry or outside funding pays for any direct cost of guideline development — it’s funded entirely by Member Institution dues
- Panel discussions are confidential; members cannot be contacted about pending changes and cannot disclose deliberations
- Every submission is voted on by the panel
- Move to abstain if involved with the studies

Takeaways



- Annual meeting by the panel is when critical changes are reviewed
- Submit strongest peer-reviewed evidence; a published manuscript is required to be considered for Category 1
- An FDA approval or urgent new evidence can trigger an interim update
- NCCN.org is your starting place
- Specialty society support critical when high level evidence is not achievable

Thank you!



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